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LYMPHOGENOUS (LYMPHATIC) LEUKEMIA

DIAGNOSTIC, PROGNOSTIC AND THERAPEUTIC CONSIDERATIONS BASED ON AN ANALYSIS OF ITS MORPHOLOGIC AND CLINICAL VARIANTS

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Lymphogenous leukemia comprises a group of pathologic states which have as their common attribute disordered and continued proliferation of lymphocyte-forming tissue not limited in response to any recognized irritant or other stimulus and manifested by continuous or intermittent alteration in the lymphocytes of the circulating blood.

Until the possible relations of leukemia to neoplastic, metabolic and infectious diseases have received greater elucidation no classification of the types of lymphogenous leukemia can be wholly satisfactory. The lack of other bases for the differentiation of leukemic lymphogenesis has led to reliance by many authors on clinical criteria, such as the apparent course of the disease and the gross regional involvement. The shortcomings of such a classification as a guide both to prognosis and to therapy are made evident by the study in retrospect of any considerable number of cases.

The application of methods for the differential staining of fixed blood films, supplemented by the oxidase reaction and supravital technics, has made possible recognition of the type of blood cell involved in the leukemic process and its approximate stage of development. Examination of circulating cells, lymph tissue and bone marrow provide grounds for the subdivision of lymphogenous leukemia. In all forms of leukemia pathologic variants of cell structure and behavior are common, but among persons with lymphogenous leukemia a distinct and persistent type of abnormality is not infrequently encountered. Such persons form a class which was first differentiated by Sternberg.[1] He observed the transformation of locally invasive lymphosarcoma into a frankly leukemic process characterized by lymphosarcoma cells in the blood stream.

Important studies descriptive of the structure of the circulating lymphosarcoma cell which serve to separate it distinctly from the lymphoblast, the young lymphocyte and the leukemic lymphocyte have been published by Wiseman [2] and by Isaacs.[3] In particular the study of blood films made on cover slips surfaced with brilliant cresyl blue and stained after drying with Wright's stain, as recommended by Isaacs, has proved of great value. Stained in this way the lymphosarcoma cell, according to Isaacs,[3] possesses

> certain differentiating features . . . the most marked being the peculiar characteristics of the nucleolus. This is usually eccentrically placed, single, very rarely multiple. . . . the nucleolus stands out as a sky blue, round area, surrounded by a deep, blue black rim of chromatin which is piled up around it. . . . In the true immature lymphocyte or lymphoblast, under these conditions, the nucleolus appears as a light blue "hole" or area in the chromatin structure, without the heavily staining rim. The nucleoli are more likely to be multiple in the immature lymphocytes or lymphoblasts than in the lymphosarcoma cell.
>
> The lymphosarcoma cell, in films, varies in size from 7.5 by 9 microns to 12 by 13.5 microns. The nucleus is usually oval or oblong, occasionally being egg shaped (thicker at one end) in films. Kidney shaped or notched forms are common in some specimens. The stained chromatin is coarsely reticular and somewhat spongy in structure and the chromatin around the edge is thickened into a fairly definite nuclear wall, differing in this respect from the monocyte. The cytoplasm of the cell is sparse, deeply basophilic, and with the brilliant cresyl blue, Wright's stain, appears as a fine, blue lace-work.

It therefore becomes possible further to classify patients with lymphogenous leukemia into three main groups on the basis of the type of lymph cell concerned in the process: the lymphoblast, the lymphosarcoma cell and the lymphocyte. Separate consideration of the group with lymphosarcoma cell leukemia clarifies many apparently conflicting observations regarding the age incidence, the clinical course and the response to roentgen therapy of persons with lymphogenous leukemia.

The material of the present study comprises all patients with leukemia observed at the Simpson Memorial Institute from 1928 to 1940 inclusive on whom the recorded data are sufficient to permit reevaluation from a diagnostic standpoint. Blood films made for practically all these patients are on file, and whenever consideration of the original observations led to reasonable doubt regarding the correct classification the films were reexamined. In all, reference was made to the films of 125 patients. The disease of approximately 10 per cent of more than 200 patients originally diagnosed as some form of lymphogenous leukemia was reclassified as myelogenous or monocytic. A few

From the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan.

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1. Sternberg, C.: Ueber Leukosarkomatose, Wien. klin. Wchnschr. **21**: 475, 1908.

2. Wiseman, B. K.: Lymphopoiesis, Lymphatic Hyperplasia, and Lymphemia: Fundamental Observations Concerning the Pathologic Physiology and Interrelationships of Lymphatic Leukemia, Leukosarcoma and Lymphosarcoma, Ann. Int. Med. **9**: 1303, 1936.

3. Isaacs, Raphael: Lymphosarcoma Cell Leukemia, Ann. Int. Med. **11**: 657, 1937.

patients were rejected entirely as having either infectious disease or carcinoma invading the blood stream. The number of persons with leukemia was 434, and of this total the patients with lymphogenous leukemia numbered 190 (43.8 per cent). Included among the latter were many patients who had provided source material for a number of earlier communications (Isaacs,[4] Rowe[5] and Friedgood[6]).

There are in this series 52 cases of lymphoblastic, 70 of lymphosarcoma cell and 68 of lymphocytic leukemia. Further subdivision has been made into subleukemic and leukemic states at the time of first observation (table 1). The criteria employed for this purpose are as follows: Subleukemic: At least 10 per cent of the circulating white cells exhibit a specific type of abnormality on which the morphologic diagnosis is based, but the total of such cells does not exceed 10,000 per cubic millimeter. Leukemic: At least 50 per cent of the circulating white cells exhibit the type-specific abnormality, and their total exceeds 10,000 per cubic millimeter. Any realistic consideration of

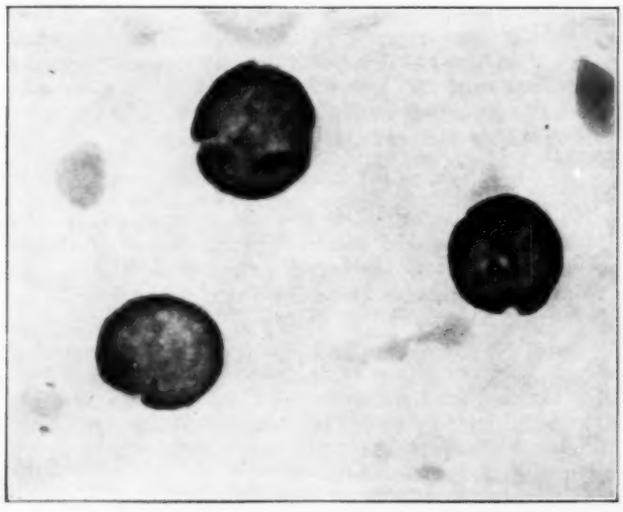

Fig. 1.—Lymphoblasts from a case of acute lymphoblastic leukemia. Figures 1, 2 and 3 are photomicrographs of cell types found in cases of lymphogenous leukemia. Cover slip blood films treated vitally with brilliant cresyl blue and stained with Wright's stain. Neutrophils and erythrocytes are shown for size comparison.

leukemia requires the relegation of quantitative changes in the circulating blood to a position of subsidiary prominence. Yet it is for patients whose disease is characterized by a leukocyte count within the usual range and by no great divergence from the normal in the distribution of cell types that accurate diagnosis becomes most difficult. All forms of lymphogenous leukemia have been observed to undergo transition from the subleukemic to the leukemic state, and vice versa, but it is in the lymphoblastic and lymphosarcoma cell types that a subleukemic picture is revealed in the majority of cases at the initial examination. The type of lymphatic hyperplasia referred to as pseudoleukemia was described by Cohnheim before present staining methods were available, and it has been found that in

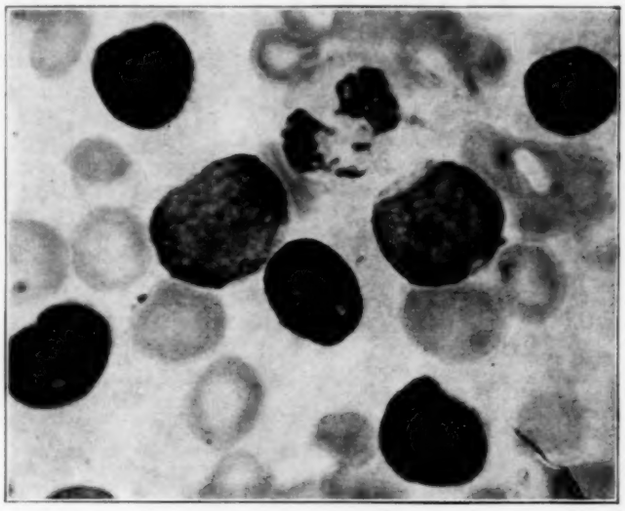

Fig. 2.—Lymphosarcoma cells from a case of subacute lymphosarcoma cell leukemia.

this disease, which may run an exceedingly chronic and benign course, there is usually a relative lymphocytosis, with at least the periodic appearance of atypical lymphocytes in the blood. Therefore it has seemed justifiable to apply the designation of subleukemia to it and to discard the term pseudoleukemia. With this view Krumbhaar[7] and Forkner,[8] among others, expressed agreement.

Pathologic examination when performed substantiated the hematologic diagnosis in all cases included

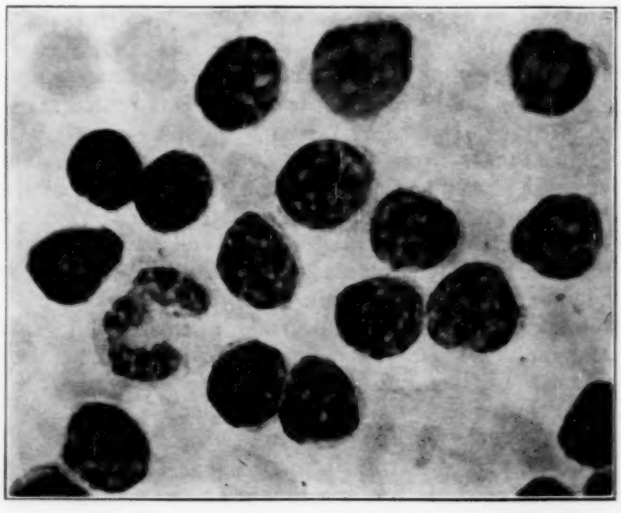

Fig. 3.—Lymphocytes from a case of chronic lymphocytic leukemia.

in this report. The number and percentage of patients who underwent various types of pathologic appraisal are shown in table 2.

The sex distribution and the age at onset of symptoms of the patients making up this study are pre-

4. Isaacs, Raphael: The Treatment of Lymphatic Leukemia, Am. J. Roentgenol. **21**: 368, 1929; Blood Changes in the Leukemias and the Lymphomata and Their Bearing on Roentgen Therapy, ibid. **24**: 648, 1930; Present Status of the Study and Treatment of Leukemia, J. Lab. & Clin. Med. **17**: 1006, 1932; Maturing Effect of Roentgen Rays on Blood-Forming Cells, Arch. Int. Med. **50**: 836 (Dec.) 1932; The Relation of Cell Types in Leukemia to Sensitivity to Radiation, Folia haemat. **52**: 414, 1934; Lymphocyte Types and Their Clinical Significance, J. A. M. A. **106**: 326 (Jan. 25) 1936; Diagnosis of Leukemia and Response to Therapy, Univ. Hosp. Bull., Ann Arbor, Mich. **4**: 129, 1938; Correlation of Clinical and Laboratory Data in Diseases of Lymph Nodes, J. Michigan M. Soc. **37**: 1072, 1938; "Notched Nucleus Cell" Leukemia, Program Cent. Soc. Clin. Research **12**: 37, 1939; Lymphosarcoma Cell Leukemia.[3]

5. Rowe, S. N.: Mikulicz's Syndrome with Chronic Lymphatic Leukemia, New England J. Med. **202**: 863, 1930.

6. Friedgood, H. B.: The Effect of Lugol's Solution on Chronic Lymphatic Leukemia and Its Bearing upon the Pathogenesis of Exophthalmic Goiter, Am. J. M. Sc. **183**: 515, 1932.

7. Krumbhaar, E. B.: The Lymphomatoid Diseases (the So-Called Lymphoblastomas), J. A. M. A. **106**: 286 (Jan. 25) 1936.

8. Forkner, C. E.: Classification and Terminology of Leukemia and Allied Disorders, Arch. Int. Med. **60**: 582 (Oct.) 1937.

sented in figure 4. Lymphoblastic leukemia is a cataclysmic disaster of childhood, occurring in the majority of cases in the first decade of life and beginning and terminating in 90 per cent before the age of 20. Two thirds of our patients were male. These data are in substantial agreement with those published by Minot and Isaacs,[9] Ward,[10] Ramsay,[11] Warren,[12] Mills,[13] Simonson[14] and others.

TABLE 1.—*Leukemic and Subleukemic Blood Pictures of Patients with Lymphogenous Leukemia*

Type of Leukemia	Subleukemic When First Observed		Leukemic When First Observed		Total Number of Patients
	Number	Percentage	Number	Percentage	
Lymphoblastic	28	53.8	24	46.2	52
Lymphosarcoma cell	44	62.9	26	37.1	70
Lymphocytic	11	16.2	57	83.8	68
Total	83	43.7	107	56.3	190

At any period of life lymph tissue may undergo sarcomatous change, and after a variable interval the neoplastic cells may break through the enclosing connective tissue and circulate freely in the blood stream. Among females no significant predilection for any age is manifest, but among males the incidence of lymphosarcoma cell leukemia appears roughly to parallel that of lymphoblastic leukemia in childhood and that of lymphocytic leukemia in mature years. It is of interest that between the ages of 10 and 40 the sexes are affected equally by lymphosarcoma cell leukemia, whereas outside these limits there is a decided predominance of males with the disease. Of the complete series 70 per cent are males.

Lymphocytic leukemia in this series was not found before the fourth decade except in 1 woman who had symptoms of the disease at 28. The age distribution agreed closely with that observed by Rosenthal and Harris[15] and by Wintrobe and Hasenbush.[16] As with the lymphosarcoma cell form women were generally affected at an earlier age than men. Sixty per cent of males were more than 60, whereas 80 per cent of females were less than 60. For the whole group with lymphocytic leukemia the percentage of men was 62, somewhat less than that observed by Ward,[10] Minot and Isaacs,[9] Leavell[17] and Wintrobe and Hasenbush.[16]

The earliest evidence of ill health in cases in which the disease subsequently was diagnosed as lymphogenous leukemia and the occurrence of various symptoms during the course of the disease are shown in tables 3 and 4. The most common early manifestations of lymphoblastic leukemia were lassitude, ease of fatigue and weakness, symptoms generally referable to anemia. In contradistinction to the observations of Warren,[12] Pierce[18] and Mills,[13] infection at the outset was noted relatively infrequently, although during the illness infections of the ears, the upper respiratory tract or the skin were observed in nearly half the cases. With both lymphosarcoma cell and lymphocytic leukemia the most common first sign of disease was enlargement of peripheral lymph nodes or the spleen, usually of the former. Throughout the course of lymphoblastic and lymphosarcoma cell leukemia, anemia, fever, hemorrhage and infection were the most conspicuous features. With the lymphocytic type fever and hemorrhage were noted much less frequently.

The duration of life after the appearance of symptoms in cases in which the date of death is known is presented in tables 5, 6 and 7. Death occurred within four months in 70 per cent of the cases of lymphoblastic leukemia, with an average survival period for the whole group of four months. The duration of lymphosarcoma cell leukemia is extremely variable, but nearly one-half the patients died within one year of the onset of symptoms or the observation of a tumor. Moreover, it is known that in this condition the first manifestation of disease usually precedes by a period of months, sometimes of years, the invasion of the blood

TABLE 2.—*Pathologic Substantiation of Diagnosis in Cases of Lymphogenous Leukemia*

Type of Leukemia	Total Number of Cases	Pathologic Examination		Necropsy		Aspiration or Biopsy of Bone Marrow Only		Biopsy of Lymph Node Only		Examination of Bone Marrow and Lymph Node Only	
		Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Lymphoblastic	52	25	48.1	16	30.8	7	13.5	1	1.9	1	1.9
Lymphosarcoma cell	70	47	67.1	18	25.7	10	14.3	16	22.9	3	4.3
Lymphocytic	68	21	30.9	8	11.8	7	10.3	4	5.9	2	2.9
Total all types	190	93	48.9	42	22.1	24	12.6	21	11.0	6	3.1

TABLE 3.—*Earliest Evidence of Ill Health in Lymphogenous Leukemia*

First Evidence of Disease	Type of Leukemia					
	Lymphoblastic		Lymphosarcoma Cell		Lymphocytic	
	Number	Percentage	Number	Percentage	Number	Percentage
Tumor of lymph glands or spleen	5	9.6	28	40.0	28	41.2
Symptoms referable to anemia	21	40.4	18	25.7	21	30.9
Evidence of infection	7	13.5	10	14.3	8	11.8
Headache	3	5.8	1	1.4	1	1.5
Pain in joints	6	11.5	1	1.4	0	0
Digestive symptoms	3	5.8	1	1.4	2	2.9
Miscellaneous pain or discomfort	0	0	1	1.4	2	2.9
Pressure of spleen or glands	0	0	3	4.3	1	1.5
Fever	4	7.7	1	1.4	0	0
Hemorrhage	3	5.8	2	2.9	0	0
Symptoms referable to increased basal metabolism	0	0	2	2.9	3	4.4
None; incidental finding	0	0	2	2.9	2	2.9
Total cases	52	100.1	70	100.0	68	100.0

9. Minot, G. R., and Isaacs, R.: Lymphatic Leukemia: Age Incidence, Duration and Benefit Derived from Irradiation, Boston M. & S. J. **191:** 1, 1924.
10. Ward, G. R.: The Infection Theory of Acute Leukemia, Brit. J. Child. Dis. **14:** 10, 1917.
11. Ramsay, G. W. S.: Leukemia in Infancy and Early Life, Arch. Dis. Childhood **2:** 119, 1927.
12. Warren, S. L.: Review of Literature and Twenty-Eight New Cases of Acute Leukemia, Am. J. M. Sc. **178:** 490, 1929.
13. Mills, S. D.: Acute Lymphatic Leukemia in Childhood: A Study of Sixty Cases with Especial Reference to the Cytologic Characteristics of the Blood, J. Pediat. **6:** 634, 1935.
14. Simonson, L. M.: Acute Leukemia in Childhood, Wisconsin M. J. **37:** 110, 1938.
15. Rosenthal, N., and Harris, W.: Leukemia: Its Diagnosis and Treatment, J. A. M. A. **104:** 702 (March 2) 1935.
16. Wintrobe, M. M., and Hasenbush, L. L.: Chronic Leukemia: The Early Phase of Chronic Leukemia, the Results of Treatment and the Effects of Complicating Infections; A Study of Eighty-Six Adults, Arch. Int. Med. **64:** 701 (Oct.) 1939.
17. Leavell, B. S.: Chronic Leukemia: A Study of the Incidence and Factors Influencing the Duration of Life, Am. J. M. Sc. **196:** 329, 1938.
18. Pierce, M.: Childhood Leukemia, J. Pediat. **8:** 66, 1936.

by lymphosarcoma cells. The duration of life in lymphocytic leukemia, although variable, was longer in this series than in others reported in the literature (Minot and Isaacs,[9] Leavell[17] and Wintrobe and Hasenbush,[16] averaging four and eighty-five-hundredths years. The difference is attributed partly to the careful exclusion

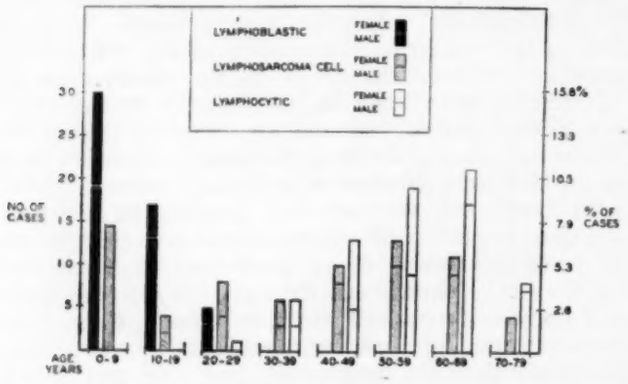

Fig. 4.—Incidence of lymphoblastic, lymphosarcoma cell and lymphocytic leukemia according to sex and age of patient at onset of symptoms.

of cases believed to represent lymphosarcoma cell leukemia and in part to efforts by the staff and the social service department to remain informed concerning the status of former patients, thus preventing many with more chronic disease from becoming lost to observation.

When observations were sufficiently frequent to justify classifying the patients according to the quantitative characteristics of the blood picture throughout the course of their illness, the duration of life from the onset of symptoms and from the date of the first observation was considered with reference to subleukemic and leukemic changes (table 8). Decreases of the leukocyte count induced by roentgen therapy were not considered in this classification. In patients with lymphoblastic and lymphosarcoma cell leukemia the duration of life was appreciably shorter in the presence of a high white cell count, whereas no such difference was observed among patients with lymphocytic leukemia.

TABLE 4.—*Symptoms Occurring During Course of Lymphogenous Leukemia*

Symptoms	Type of Leukemia: Lymphoblastic Number	Lymphoblastic Percentage	Lymphosarcoma Cell Number	Lymphosarcoma Cell Percentage	Lymphocytic Number	Lymphocytic Percentage
Symptoms referable to anemia	52	100.0	64	91.4	55	80.9
Susceptibility to infection	25	48.1	39	55.7	28	41.0
Headache	7	13.5	17	24.3	9	13.2
Pain in joints	11	21.2	4	5.7	0	0
Symptoms referable to gastrointestinal tract	10	19.2	16	22.8	13	19.1
Miscellaneous pain or discomfort	5	9.6	4	5.7	11	16.2
Pressure of glands	9	17.3	20	28.6	17	25.0
Pressure of spleen	2	3.8	6	8.6	8	11.8
Fever	44	84.6	43	61.4	12	17.6
Hemorrhage	39	75.0	27	38.6	13	19.1
Symptoms referable to increased basal metabolism	0	0	12	17.1	16	23.5
None	0	0	0	0	2	2.9

The immediate causes of death among 86 patients with lymphogenous leukemia are shown in table 9. The greatest hazard to life in lymphocytic leukemia is the susceptibility to infection, particularly pneumonia, but for patients with this disease, including many elderly persons, there is at least one chance in three of dying of a cause wholly unrelated to leukemia.

Differentiation of lymphogenous leukemia according to the morphologic characteristics of circulating leukemia cells aids in the decision regarding the suitability of roentgen therapy and contributes to the determination of the dose, the number of treatments and the regions of the body to receive treatment. A summary of the results obtained from roentgen therapy is presented in table 10. In the evaluation of data, when more than one course of therapy was employed the most favorable response was selected.

The experience gained from this series is in agreement with that of Stengel and Pancoast,[19] Minot and Isaacs,[9] Simonson[14] and others in demonstrating the negative and often harmful effects of radiation therapy for lymphoblastic leukemia. Therefore I feel justified in withholding this form of treatment from patients with the disease, even when urged to employ it by their relatives.

In the management of lymphocytic leukemia roentgen therapy has proved of much greater value than the use of arsenicals or any other form of treatment employed.

TABLE 5.—*Duration of Lymphoblastic Leukemia After the Appearance of Symptoms in Forty-Seven Cases: Average Duration, Four Months*

	Months: 0-2	3-4	5-6	7-8	9-10	11-12
Number of cases	15	18	6	4	2	2
Percentage of cases	31.9	38.3	12.7	8.5	4.3	4.3

TABLE 6.—*Duration of Lymphosarcoma Cell Leukemia After the Appearance of Symptoms in Sixty-One Cases: Average Duration, Thirty-One and Three-Tenths Months*

	Years: 0	½	1	2	3	4	5	6	7	8	9	10
Number of cases	17	13	9	6	2	3	2	3	3	1	1	1
Percentage of cases	28.0	21.3	14.8	9.8	3.3	4.9	3.3	4.9	4.9	1.6	1.6	1.6
	49.3											

The usual procedure has involved the use of 200 kilovolts and a dose per treatment of 150 to 200 r measured in air to ports ranging from 10 by 10 to 15 by 15 cm. A series of daily treatments numbering usually eight to twelve is applied regionally to the peripheral lymph node areas, the mediastinum, the retroperitoneal region and the spleen. The indications for therapy are anemia, debility, evidence of increased metabolism, pressure symptoms and, least important, a progressive rise in the leukocyte count. The interval between courses of therapy is made as long as possible. Anemia and thrombocytopenia do not militate against the effectiveness of roentgen therapy in cases of lymphocytic leukemia except as they may be part of the terminal cachexia of the disease. Many patients retain the property of responding to roentgen therapy, given many times over a period of years. It appears that ultimate failure to respond depends not so much on an acquired "refractory" state, brought about by previous therapy, as on the progressive nature of the disease, often characterized by increasing proliferation of young lymphocytes and lymphoblasts.

19. Stengel, A., and Pancoast, H. K.: The Treatment of Leukemia and Pseudoleukemia with X-Rays, J. A. M. A. **59**: 1166 (Sept. 28) 1912.

Greater caution is needed in the treatment of lymphosarcoma cell leukemia than in that of lymphocytic leukemia, and the results generally are less satisfactory. In patients with lymphosarcoma cell leukemia an exceedingly rapid decrease in the white cell count after irradiation is common and there may be associated

TABLE 7.—*Duration of Lymphocytic Leukemia After the Appearance of Symptoms in Thirty-Three Cases: Average Duration, Fifty-Eight and Two-Tenths Months*

	Years									
	1	2	3	4	5	6	7	8	9	10
Number of cases	4	2	6	7	3	2	4	2	1	2
Percentage of cases	12.1	6.1	18.2	21.2	9.0	6.1	12.1	6.1	3.0	6.1

SUMMARY AND CONCLUSIONS

A series of 190 cases of lymphogenous leukemia subdivided into cases of lymphoblastic, lymphosarcoma cell and lymphocytic leukemia on the basis of the morphologic characteristics of the pathologic lymph cells in the circulating blood, is analyzed with respect to age and sex incidence, symptoms, duration of life and response to therapy.

Lymphoblastic leukemia is a disease of childhood, affecting twice as many males as females and characterized by anemia, fever, a tendency to uncontrollable hemorrhage and susceptibility to infection. Its duration is usually less than four months, and its course in most cases is either uninfluenced or adversely affected by roentgen therapy.

Lymphosarcoma cell leukemia is a distinct morphologic and clinical entity, characterized by the presence of lymphosarcoma cells in the blood stream. Males are predominantly affected, and the disease may occur at any age. After the development of a leukemic blood picture the course is usually rapid, but in some cases roentgen therapy cautiously employed exerts a noticeably beneficial effect.

Lymphocytic leukemia affects more males than females and occurs almost exclusively in the middle and later years of life. Its course may be relatively benign and is usually favorably influenced by roentgen therapy.

The prognosis and therapeutic indications cannot safely be based solely on morphologic characteristics of the affected cells, but the histologic condition of the blood and the blood-forming organs as a whole, considered in conjunction with the clinical features, provides a basis for a plan of treatment and a reasonably accurate prediction of the course of the disease.

TABLE 8.—*The Duration of Life in Patients with Lymphogenous Leukemia Observed Until Death, Classified According to Quantitative Changes in Circulating Leukemic Cells*

		Subleukemic Throughout			Leukemic Throughout			Subleukemic Becoming Leukemic			Leukemic Becoming Subleukemic			Alternating Subleukemic and Leukemic		
Type of Leukemia	Total Cases	A* %	B Mo.	C Mo.	A %	B Mo.	C Mo.	A %	B Mo.	C Mo.	A %	B Mo.	C Mo.	A %	B Mo.	C Mo.
Lymphoblastic	37	29.7	4.5	1.5	29.7	2.9	0.8	16.2	3.3	1.5	10.8	5.0	2.0	13.5	4.4	2.0
Lymphosarcoma cell	40	42.5	26.1	15.4	25.0	12.3	2.4	17.5	14.4	7.4	5.0	51.0	41.0	10.0	55.5	23.8
Lymphocytic	25	8.0	52.0	22.0	76.0	52.6	23.4	4.0	12.0	9.0	12.0	60.0	48.7	0	0	0

* Column A in each group gives the percentage of cases, column B the average duration after the onset of symptoms and column C the average duration after the first observation.

TABLE 9.—*Immediate Cause of Death in Cases of Lymphogenous Leukemia*

	Toxemia		Hemorrhage		Infection		Debility		Unrelated Cause		Total
Type of Leukemia	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number
Lymphoblastic	22	71.0	8	25.8	1	3.2	0	0	0	0	31
Lymphosarcoma cell	15	46.9	2	6.2	9	28.1	3	9.4	3	9.4	32
Lymphocytic	0	0	1	4.3	8	34.8	6	26.1	8	34.8	23
Total all types	37	43.0	11	12.8	18	20.9	9	10.5	11	12.8	86

TABLE 10.—*Response to High Voltage Regional Roentgen Therapy in Cases of Lymphogenous Leukemia*

		Unfavorable*		None		Fair		Good		Very Good		Excellent	
Type of Leukemia	Total Number	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Lymphoblastic	10	3	30.0	4	40.0	3	30.0	0	0	0	0	0	0
Lymphosarcoma cell	47	11	23.4	8	17.0	13	27.7	6	12.8	4	8.5	5	10.6
Lymphocytic	43	0	0	2	4.7	6	15.8	9	20.9	10	23.3	16	37.2

* Unfavorable, exacerbation of leukemic process with early death; none, course of disease apparently unaltered; fair, transient clinical improvement but no real remission; good, significant clinical and hematologic improvement lasting 3 to 6 months; very good, significant clinical and hematologic improvement lasting 6 to 12 months; excellent, significant clinical and hematologic improvement lasting more than 12 months.

severe toxic symptoms. Localized therapy directed only toward the relief of pressure manifestations is often advisable for such patients, but some derive prolonged benefit from roentgen therapy to all of the major regions of lymphatic tissue.

Other means of treatment which have been used with some success on a few patients with lymphocytic or lymphosarcoma cell leukemia include liver preparations administered orally and parenterally, compound solution of iodine (Lugol's solution) and solution of potassium arsenite (Fowler's solution), the last-mentioned remedy in doses gradually increasing to 30 minims (1.8 cc.) administered daily or until toxic effects are observed. In the treatment of lymphoblastic leukemia symptomatic relief is all that is attempted and reliance is placed chiefly on blood transfusion, which in some cases results in transient reduction of activity of the leukemic process.

LYMPHATIC LEUKEMIA

IMPORTANT FACTS ADDITIVE TO ITS CLINICAL AND HEMATOLOGIC RECOGNITION

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COLUMBUS, OHIO

Progress in medicine always has depended primarily on the solution of the basic problem of the mechanism of the production of disease. In some fields, as for example that of infectious diseases, the basic factors are known in quantity sufficient to provide diagnosis and treatment on a plane of efficiency which removes many of them from a position of threat to longevity. In other fields, however, so few of these factors are known that any attempt to reconstruct the mechanism of these diseases can result in nothing more acceptable than a working hypothesis, with all the limitations that this implies. Nevertheless, such working hypotheses, provided that they are founded on facts, even if there are few, are fundamentally important in laying a foundation on which construction, and in certain details perhaps reconstruction, may lead to a universally acceptable account of the mechanism of the disease. Additionally, of immediate practical value, a system of thought the elements of which do not violate the facts observed in the clinic and laboratory aids materially in the recognition, treatment and prognosis of the disease.

Specifically, these principles have been applied to the problem of the primary diseases of the lymphatic tissues. The present paper summarizes in broad perspective a working hypothesis applicable to a sounder understanding of these dyscrasias as seen in the clinic. It is important to add that whatever shortcomings in this hypothesis may be revealed by future investigations, the theory works in the clinic and makes possible exact identification, better treatment and a more reasonable prognosis than was hitherto possible. Because this hypothesis works in practice, it is not felt that this fact, obversely stated, detracts from the possible soundness of the theory.

NOMENCLATURE

From any point of view, the terms lymphoma and lymphoblastoma to designate any of the primary diseases of the lymphoid tissues do not appear desirable. The use of either serves (1) to deny that there is any virtue in trying to determine the mechanism of the production of the several types of lymphoid diseases, (2) to deny that there is any fundamental difference between them or (3) to constitute prima facie evidence of the technical inability of the diagnostician (or pathologist) to differentiate between them. Of these three inferences, the latter is the only one that might be acceptable. When so used, the diagnosis should be construed by the interested parties on this basis and not in a sense that further dissection of the exact nature of the process is futile and of no theoretical or practical value. For example, a case of lobar pneumonia might be labeled as one of "infectious disease" rather than "lobar pneumonia, pneumococcus type I." The charge is made here that this use of the term, while not essentially incorrect, is too broad and conveys too little.[1]

A final statement on the nomenclature of the lymphatic diseases includes the fact that while descriptive pathology may justify a variety of terms, a thorough study of the clinical diseases in this category indicates that the terms lymphosarcoma, leukosarcoma and lymphatic leukemia (including the type of Cohnheim) are accurate and adequate to embrace all the now known types of noninfectious primary lymphocyte dyscrasias. Lymphatic leukemia without lymphemia is of course a contradiction unless one defines the term leukemia as a disease entity without the original implication of leukemia meaning "white blood."

MECHANISM OF PRODUCTION OF THE PRIMARY LYMPHATIC DISEASES

A survey of the known facts concerning the growth characteristics of cells shows that multiplication of these elements is determined by two, and only two, factors, namely maturation and division. Abnormalities in the growth of cells therefore theoretically must be modification in the participation of these two factors acting singly or together. It is therefore possible to construct a list of the theoretically possible lymphoid diseases and compare these with the forms of lymphoid diseases actually observed in the clinic. A diagrammatic representation of this relationship is shown in figure 2. In the center of the circle the origin of the lymphocyte is shown from the reticular cell, the definitive circulating cell achieving its mature form through successive stages of maturation and division. Normally maturation and division occur simultaneously; if either is interfered with, diseases primarily involving the lymphocyte are theoretically possible.

As shown in figure 2, this works out theoretically to give three types of hyperplasia—one with normal lymphocytes and two with immature lymphocytes, the cells of both showing defects in maturation but only one showing neoplastic features. The placing of the diseases in this figure corresponding with the mechanism that is suggested as at fault results from a detailed study of the clinical entities named, all available criteria being applied which have come into my possession from ten years of study in this field. Briefly stated, when the lymphocytes produced in the course of the several types of primary lymphatic diseases are assayed for evidences of maturation with the criteria previously published,[10] it is found that maturation proceeds according to and parallel with the numerical fluctuations in the lymphocytes (in consonance with the speed of production) only in the lymphopoiesis of the known infectious states (fig. 3[11]). The lymphocytes in chronic lymphatic leukemia do not show abundant maturative phenomena when large numbers of cells are being produced (fig. 4[12]). Neither do they possess certain features regularly seen in neoplasia in general. On the other hand, the lymphocytes in cases of acute lymphatic leukemia and of lymphosarcoma, either with or without

From the Department of Medicine, Ohio State University College of Medicine. Supported in part by a grant from the Cowley Fund.

Read before the Section on Practice of Medicine at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

Because of lack of space, this article is abbreviated in THE JOURNAL by the omission of some illustrations, tables and text. The complete article appears in the author's reprints.

1. A detailed discussion of nomenclature appears here in the author's reprints.

10. Wiseman, B. K.: Criteria of the Age of Lymphocytes in the Peripheral Blood, J. Exper. Med. **54**: 271, 1931.

11. Wiseman, B. K.: Lymphopoiesis, Lymphatic Hyperplasia, and Lymphemia: Fundamental Observations Concerning the Pathologic Physiology and Interrelationships of Lymphatic Leukemia, Leukosarcoma and Lymphosarcoma, Ann. Int. Med. **9**: 1303, 1936.

12. Wiseman, B. K.: The Lymphadenopathy Problem in Blood, Heart and Circulation: Symposium, Publication 3, American Association for the Advancement of Science, 1940, p. 20.

leukemic blood (leukosarcoma), while also not showing the maturative phenomena expected, do possess all the attributes of neoplastic cells. On the basis of these observations, therefore, it would appear that figure 2 should be completed as shown.

TABLE 4.—*First Mechanism of Production of Lymphatic Leukemia*

Localized Origin (neoplastic)

Without Lymphemia (lymphosarcoma) → With Lymphemia (acute lymphatic leukemia "leukosarcoma")

Facts in Support of Neoplastic Mechanism

1. Acute course < 1 year
2. Two types of lymphocytes
3. Frank metastasis observed in lymph nodes
4. Mitosis > 5/1,000; average 18/1,000
5. Radiosensitivity 4+
6. Tissue culture → neoplastic features
7. Micrometabolism → neoplastic type

Diagrammatically summarized, this indicates that lymphatic leukemia, when neoplastic in origin, begins in a localized focus of neoplastic lymphocytes, either immediately characterized in the blood by lymphemia or after an indeterminate period during which time blood examinations appear normal.

With this approach, all diseases that are primary in the lymphocyte belong in one of these three categories, and if these categories are in fact separate and distinct entities, as suggested by the completion of figure 2, they should as groups present distinct characteristics of various kinds. This is found to be true, as analysis of many cases of each of the three groups shows distinctions in the clinical course, autopsy findings, condition of the cells, microscopic examination, radiosensitivity, tissue culture and micrometabolism of the lymphocytes as summarized in table 1. The factual data supporting this concept have previously been published.[12a]

THE CLINICOHEMATOLOGIC ASPECTS OF LEUKEMIA

The preceding discussion suggests that, when studied carefully, all the primary noninfectious diseases of the lymphocyte are basically states of leukemia. When definite lymphemia is present, there is little difficulty in identification of the type of lymphoid disorder. Thus, lymphosarcoma with lymphemia (leukosarcoma, "acute lymphatic leukemia") and lymphatic leukemia with lymphemia ("chronic lymphatic leukemia") do not ordinarily present difficult diagnostic problems. In contrast, lymphosarcoma without lymphemia and lymphatic leukemia without lymphemia are identified usually by recourse to diagnostic measures in addition to a simple examination of the peripheral blood.

TABLE 5.—*Sixty-Six Cases of Lymphosarcoma-Leukosarcoma*

Distribution by sex: male 40, female 26		
Distribution by age: range from birth to 65 years (0-10) 25, (10-20) 10, (20-30) 8, (30-40) 9, (40-50) 7, (50-60) 4, (60-70) 3		
Clinical onset:		
Fatigue syndrome (including pallor and adenopathy)	32	"P. A."
Adenopathy alone	6	
Hemorrhage and/or purpura	12	"purp. hemorrhagica"
Gastric (chiefly nausea and vomiting)	6	} acute surgical condition in abdomen
Abdominal pain	3	
Rheumatic (including bone pain)	6	"arthritis"
Upper respiratory infection	5	coryza
Dyspnea (obstruction)	2	

This summarizes the distribution by age and sex of 66 consecutive patients with lymphosarcoma and leukosarcoma, together with the symptoms or signs, by groups, at the onset of the disease. In the right hand column is indicated the most common diagnosis (when wrong) made by the referring physician.

Lymphosarcoma With and Without Lymphemia.—The present disorder in nomenclature and the indefinite criteria used in determining a tissue diagnosis in the lymphatic diseases make it impossible to compare the experience of one clinic with that of another. For example, lymphosarcoma usually means one thing to one group (with the microscopic examination, condition of the blood, clinical course and all the rest varying accordingly) and something else to another. However, if care is exercised in disqualifying for this category all lymphoid tumors that involve primarily the reticulum cell (including Hodgkin's disease) and the pseudoleukemia of Cohnheim, our experience indicates that there are few cases of lymphosarcoma, if any, which do not eventually terminate in leukemia and which run a clinical course exceeding one year. The foregoing state-

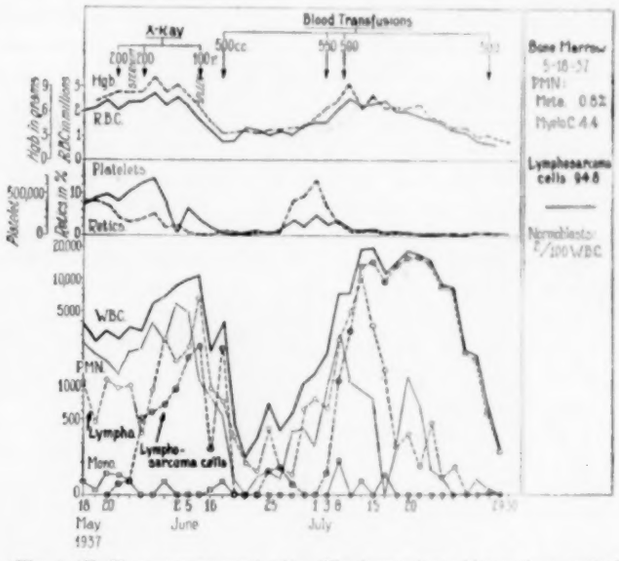

Fig. 1 (E. H., a woman aged 43).—The hematologic history in a typical case of lymphosarcoma-leukosarcoma. Note that the "sarcoma" lymphocytes were not found in the peripheral blood during three periods (May 18, 20-June 21, 24-June 30, July 1). Between these periods on two occasions the values for these cells rose to high levels. At all times, however, the sternal bone marrow was composed chiefly of the pathologic lymphocytes. Interesting also is the terminal leukopenia in which the sarcoma cells constituted practically 100 per cent of the circulatory white blood cells. Charting is on a semilogarithmic scale. A section of a lymph node is illustrated in 5 and 6, figure 5.

ments adequately explain the entirely dissimilar conclusions found in different publications; for example, in a recent paper from the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City,[18] only 6.6 per cent of the patients diagnosed (histologically) as having lymphosarcoma showed blood changes of leukemia, and of all the patients so diagnosed there was a five year survival rate of 10.6 per cent. Since of the 196 cases reviewed, 184 were said to be of the reticulum cell "lymphosarcoma" type, it would appear that an indeterminate but only small number of those reported can rigidly be classed as diseases of the lymphocyte itself. Histologically, in this clinic the term lymphosarcoma is confined to lymphoid dyscrasias in which the cell primarily involved can be identified as the lymphocyte and shows morphologic alterations

12a. Wiseman.[12] A summarization of these data is given in the author's reprints.

18. Sugarbaker, E. D., and Craver, L. F.: Lymphosarcoma, J. A. M. A. **115**: 17 (July 13) 1940.

of the neoplastic type (previously described [11]). These tissues are rich in lymphocytic mitoses and show no increase in fibrous tissue.

When lymphosarcoma is restricted to this category, it is my experience that all cases of lymphosarcoma are basically leukemic states, neoplastic in origin and running an acute or subacute course. In my opinion this type of leukemia corresponds to the leukemia seen in laboratory animals and, for the reasons stated earlier in this paper, is fundamentally different from "chronic lymphatic leukemia." A summarization of this concept is shown in table 4.

My experience with this disease comprises 66 cases. The distribution by age and sex with the observed types of clinical onset are condensed in table 5. Almost half of these cases initially show severe anemia, often without associated adenopathy or splenomegaly. The peripheral blood when altered is myelophthisic and/or leukemic, often resembling when not leukemic that seen in pernicious anemia. Aspiration of a sample of sternal bone marrow reveals that most of the marrow tissue is replaced with neoplastic lymphocytes and, particularly in the early phases of the disease, there is often no detectable invasion of the peripheral blood with these abnormal cell forms (fig. 1). Later when lymphemia occurs samples of the peripheral blood show that the increase in white blood cells is due solely to neoplastic lymphocytes, although normal lymphocytes may always be identified, often in the same oil immersion field of the microscope, side by side with the pathologic cells. Figure 1 [19] shows the hematologic course of events in 1 of these patients with a typical clinical and hematologic picture of pernicious anemia, even to a histamine-refractory achlorhydria. There was no adenopathy or splenomegaly. An aspirated sample of bone marrow, however, permitted identification of the disease when every other available method of examination failed.

Fig. 2.—The primary diseases of the lymphocyte. Theoretically possible types of reactions of the lymphocyte with the diseases thereby produced. The second zone from the center indicates hyperplasia or hypoplasia induced by suppression of maturation and/or division occurring during the life cycle of the lymphocyte shown diagrammatically in the center. The type of disease produced by these tissue reactions is suggested in the next to the outer zone, with the type of blood reaction summarized in the outermost zone.

19. All high voltage roentgen therapy of patients in this communication was given under direction of Dr. Hugh Means, roentgenologist to the University Hospital. All blood counts were made by the supravital technic.

Later, as shown, the blood stream showed invasion with pathologic lymphocytes of the neoplastic type. Attention is also directed to the severe thrombocytopenia that (characteristically) developed in this patient. As figure 1 indicates, excessive thrombocytopenia may be the chief early developing feature of this disease and accounts for the fact that hemorrhage and/or purpura in our series was the second most common presenting onset of this type of leukemia. Most cases of this variety of leukemia exhibiting hemorrhage have been referred to us as cases of essential thrombocytopenic purpura. Usually examination of the blood but often of the bone marrow is necessary to clear up the diagnosis. The third most common onset consists of abdominal symptoms, occasionally with the urgent decision to be made for or against immediate surgery. One of the patients in this summary table presented a classic syndrome of acute appendicitis. It is our belief that the origin of these symptoms are attributable to hemorrhage in various tissues determining the localization of symptoms within the abdomen, since all showed low values for blood platelets. Joint pain, bone pain and onsets with "upper respiratory infections" were next most common as the initial presenting clinical features in our series. Two of the latter were felt to be cases of granulocytopenia by the referring physician because of the very low value for peripheral circulating granulocytes. Dyspnea was the presenting symptom in 2 cases of this series. One of these revealed a large mediastinal mass without anemia, thrombocytopenia or neutropenia and without evidence in the peripheral blood of pathologic lymphocytes (fig. 3). In this instance aspiration of bone marrow on the patient's admission to the hospital on November 22 showed only 16 per cent of the marrow elements to be lymphosarcoma cells. This was twelve days before the abnormal types of lymphocytes were found in the peripheral blood.

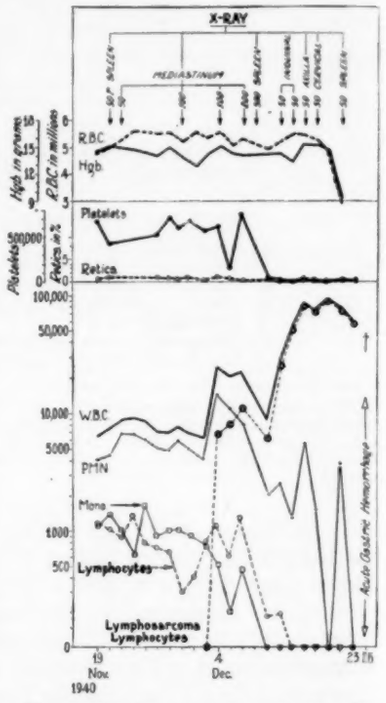

Fig. 3 (H. P., a youth aged 16).—The hematologic history in a case of lymphosarcoma which eventually terminated in leukosarcoma. The plotting is on a semilogarithmic scale. Attention is directed to the plotting of two curves for the lymphocytes; when the lymphatic tissue became infiltrated extensively with the lymphosarcoma cells, the normal lymphocytes disappeared from the peripheral blood. This is comparable to the mechanism that produced the thrombocytopenia. The course of the disease was probably too rapid for the reflection of anemia in the peripheral blood except terminally, as red blood cells have a life period of at least thirty days. Note also the parallel fall in granulocytes and normal lymphocytes at the same time that the platelets disappear.

Attention is also called to a feature on this chart showing that lymphemic levels of 95,000 "sarcoma" cells per cubic millimeter of blood were obtained rapidly after an abrupt rise. Whether lymphemia is induced by roentgen therapy, as has been suggested,[4] is not

known. The late precipitous fall in red cells preceded by near zero platelet levels reflects the increased degree of infiltration of the bone marrow with lymphosarcoma cells, as examination at this time showed the bone marrow tissue to be almost completely replaced with this type of pathologic cell. The terminal gastric hemorrhage is attributed to the almost complete absence of platelets from the blood stream.

It is again emphasized that the diagnosis of this type of leukemia before lymphemia appears is often impossible without recourse to study of the bone marrow. When peripheral adenopathy is present, biopsy is an additional aid and reveals a variable amount of replacement of the lymph node with sheets of pale staining cells rich in mitosis, often interspersed with islands of normal lymphocytes. The diagnostic features of this variation of lymphosarcoma is summarized in table 6.

Lymphatic Leukemia.—The second mechanism that results in lymphatic leukemia bears little resemblance to that of the series of cases just cited. Other than the assumption, not supported by facts, that the leukemia of laboratory animals is identical with that occurring in man, there is little reason to believe that "chronic" lymphatic leukemia is neoplastic in origin. On the other hand, there is an appreciable amount of data that this form of leukemia is neither infectious nor neoplastic. By elimination of these two suggested etiologic theories an obscure metabolic origin would be not at all improbable. Table 7 summarizes diagrammatically my concept of a second mechanism for the production of leukemia of the benign lymphatic type.

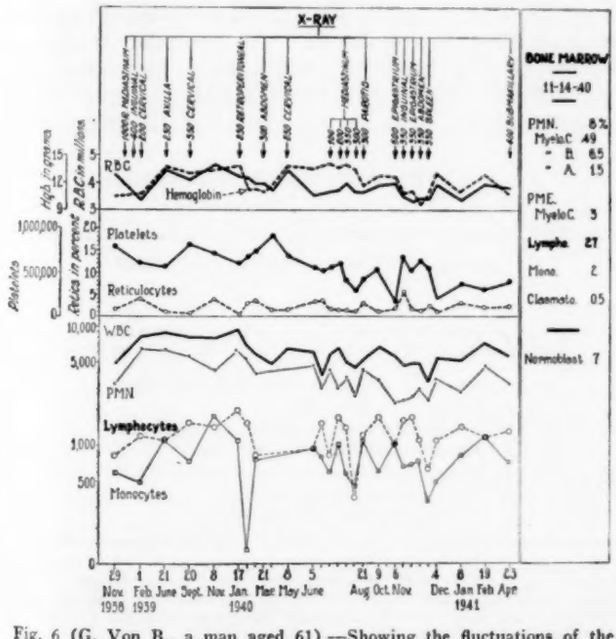

Fig. 6 (G. Von B., a man aged 61).—Showing the fluctuations of the blood elements with high voltage roentgen treatment in case of lymphatic leukemia without lymphemia followed over a period of two and a half years. The charting is on a semilogarithmic scale. A typical sternal bone marrow differential is shown as of Nov. 11, 1940, after 1,900 r of high voltage therapy.

Lymphatic Leukemia with Lymphemia ("Chronic Lymphatic Leukemia").—Illustrative material and cases centering about this variety of lymphatic leukemia has been the subject of many papers which have been well summarized by Forkner.[20] When lymphemia is present or when there is a specific alteration in the differential count a diagnostic problem is not usually encountered. Transitions between lymphatic leukemia with lymphemia and the variety without lymphemia are occasionally seen. One such case is illustrated in figure 4.

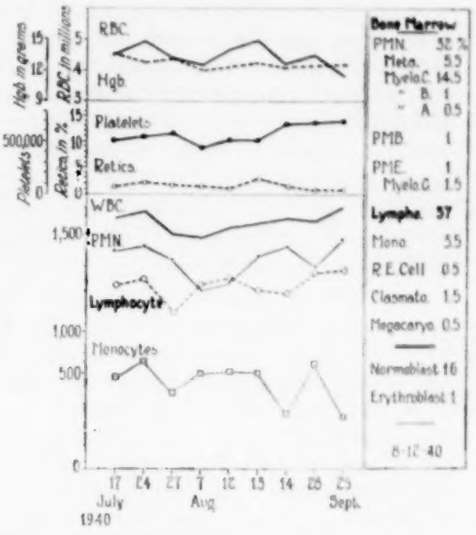

Fig. 8 (A. S., a woman aged 32, with onset at 13 years).—Showing that, exceptionally, even after twenty years of lymphatic leukemia (type Cohnheim) there may be no quantitative alterations of the cellular elements in the peripheral blood, and only moderate infiltration in the sternal bone marrow. Semilogarithmic scale.

Lymphatic Leukemia Without Lymphemia (Type Cohnheim).—This is the type of lymphoid disease that is usually diagnosed as "lymphosarcoma," "lymphocytoma," occasionally "follicular lymphoblastoma" (although this histology is unusual in lymphatic leukemia) and of course many times by the broad terms "lymphadenoma," "lymphoma" and "lymphoblastoma." With rare exceptions, the microscopic appearance of the lymphatic tissues is identical with that of lymphatic leukemia with lymphemia, but the blood shows either no distortions or only minor ones in the total number of white blood cells and/or differential. On close inspection, however, qualitative changes in the lymphocytes of the peripheral blood may usually be noted, these changes being identical with those seen in lymphatic leukemia with lymphemia. The importance of according recognition to this type of leukemia, aside from the theoretical implications, lies in the fact that not only may the clinical course and the longevity of the illness be predicted with reasonable certainty, but also more exact and adequate therapy can be given. In this type of leukemia it is especially important to understand that therapy should be directed toward the fundamental disease and not to the blood count, as illustrated by the preceding case (fig. 4). Because of the practical importance of this form of leukemia, several cases will be cited.

Figure 6 shows graphically the hematologic course in a typical case in which therapy is given. The patient was admitted to the University Hospital with the chief complaints of unsightly generalized enlargement of the lymph nodes and shortness of breath. The clinical onset occurred one year prior to hospitalization, at which time only dyspnea on exertion was noted. Four months before admission to the hospital he began experiencing dyspnea while at rest and complained of a dry, nonproductive cough. A chest plate, on admission

20. Forkner, C. E.: Leukemia and Allied Disorders, New York, Macmillan Company, 1938.

to the hospital, showed a large mass in the right middle and upper part of the mediastinum. The basal metabolic rate was plus 23 per cent. The blood count was substantially normal (fig. 6) except that qualitative alterations in the lymphocytes of a character commonly seen in lymphatic leukemia were noted. Biopsy of a lymph node showed the typical changes of lymphatic leukemia. Examination of a specimen from the sternal bone marrow showed 36 per cent of the marrow cells to be lymphocytes, all possessing the qualitative characteristics of the lymphocytes of lymphatic leukemia. The remainder of the laboratory data was not pertinent. High voltage roentgen therapy was given to the mass in the mediastinum as follows: November 30, to an anterior port 15 cm. in diameter, 150 r was directed; December 1, to an anterior port 15 cm. in diameter, 200 r; December 3, to

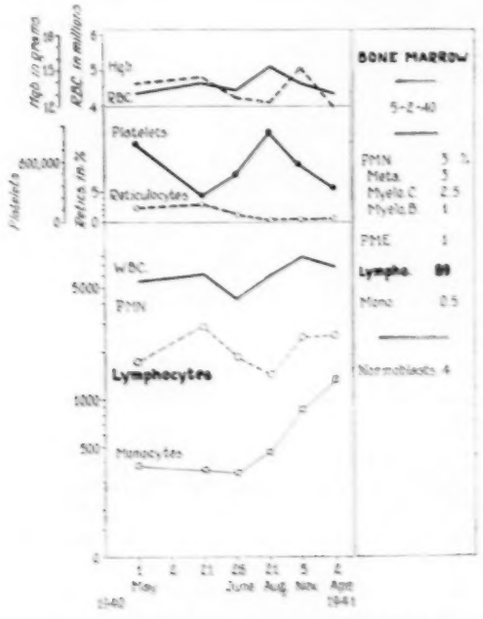

Fig. 9 (K. T., a woman aged 40).—The hematologic history is shown on this chart in a case of lymphatic leukemia (Cohnheim) in which a high degree of infiltration by lymphocytes in the sternal bone marrow persists without depreciation in the peripheral blood elements. This degree of marrow infiltration usually, but as shown here not necessarily, predisposes to myelophthisic peripheral blood. The patient is also symptom free and presents only minimal adenopathy and splenomegaly. Roentgen treatment has not been necessary. The plotting is on a semilogarithmic scale.

a posterior port 15 cm. in diameter, 300 r; December 5, to a right anterior port 15 cm. in diameter, 350 r. Following this, 400 r was given to the right and left inguinal lymph nodes. Further treatment was subsequently given as shown on the chart. Following the high voltage roentgen therapy of the mediastinum, the original mass could not be visualized and all respiratory symptoms disappeared. Three weeks later the basal metabolic rate was plus 5. It is interesting to observe that no particular depression of the lymphocytes occurred in the peripheral blood, although an appreciable effect is observed on the red blood cells. Subsequent treatments with high voltage therapy show that, other than a transient anemia and mild thrombocytopenia, no adverse effects are produced in the blood, in the bone marrow or in the patient. Symptomatically, the patient each time was rehabilitated and the bone marrow reflected decreasing infiltration with lymphocytes. A typical bone marrow count is shown on the chart under date of Nov. 14, 1940, in which, after a series of radiation treatments, as indicated, the lymphocyte count in the bone marrow was 27 per cent of the marrow cells, as compared with a value of 58 per cent prior to this course of radiation therapy.

Figure 8 is particularly instructive in that it illustrates the extreme chronicity in some cases of lymphatic leu-

TABLE 6.—*Atypical Lymphatic Leukemia*

[Mechanism: Lymphosarcoma Without Lymphemia]
Diagnosis:
1. Clinical:
No decisive points; extremely radiosensitive; often no adenopathy or splenomegaly; usually no fever or weight loss
2. Hematologic:
Blood picture.—Always myelophthisic in type with hyperchromic macrocytic anemia and variable severity of thrombocytopenia and neutropenia
Bone marrow.—Aspiration shows variable replacement with neoplastic lymphocytes
3. Biopsy: Variable degree of metastasis occurs

A summarization of the chief diagnostic facts in cases of lymphosarcoma when lymphemia is not apparent.

kemia without lymphemia entirely comparable to the chronicity in cases of lymphatic leukemia with lymphemia previously referred to. A. S. had received high voltage roentgen therapy intermittently to control the enlargement of lymph nodes for nineteen years. The onset was at least as early as the age of 13 years, which demonstrates that this disease is not necessarily more rapid in progression in youth than in old age. The patient shows a normal peripheral blood count except for the qualitative changes in the lymphocytes that always characterize this disease. A lymph node removed at biopsy Aug. 22, 1940 revealed the typical microscopic appearance of lymphatic leukemia. An aspirated sample of sternal bone marrow reflected a mild infiltration with qualitatively altered lymphocytes (37 per cent of the marrow cells). Usually not more than 10 per cent of

TABLE 7.—*Second Mechanism of Production of Lymphatic Leukemia*

Generalized Origin (probably not neoplastic)	
↓	↓
Without Lymphemia (pseudoleukemia of Cohnheim)	With Lymphemia (chronic lymphatic leukemia)
Facts in Conflict with Neoplastic Mechanism	
1. Course 3 to 25+ years	
2. Lymphocytes—morphology not neoplastic	
3. Mitosis—rare; divide by amitosis	
4. Radiosensitivity—⅓ of lymphosarcoma	
5. Tissue culture—normal cells	
6. Micrometabolism—not neoplastic	

Diagrammatically summarized, this indicates that, when lymphatic leukemia is not the result of neoplastic changes in the lymphocyte, the fundamental alteration in the lymphoid tissues occur simultaneously throughout the body; in some instances the lymphocytes are increased in the blood, in other cases not.

the marrow cells in normal sternal bone marrow are lymphocytes, and these do not show qualitative morphologic changes. The patient continues to be in apparently perfect health and suffers the only inconvenience of occasional trips to the x-ray treatment room for reduction in size of unsightly lymph nodes.

Figure 9, which charts the course of K. T., in contrast to the preceding charts, shows advanced bone marrow infiltration with lymphocytes (89 per cent of the marrow cells), although the peripheral blood shows

no quantitative alterations, relative or absolute, of the lymphocytes contained therein. This case illustrates particularly (1) the degree of lymphocytic infiltration which may be present in the bone marrow without producing a progressive anemia, thrombocytopenia or clinical symptoms, a fact contrary to the usual experience, and (2) that, with generalized adenopathy, a lymphatic system with the characteristic changes of lymphatic leukemia (a biopsy was accomplished May 2, 1940) and a high degree of infiltration in the bone marrow, there has been no increase in numbers of lymphocytes in the peripheral blood over a period of observation of more than one year.

The diagnosis of lymphatic leukemia without lymphemia (type Cohnheim) is not difficult. Clinically the important feature is the presence of long-standing adenopathy, generalized and often massive, in a patient without complaints except possibly those due to pressure by some particularly large mass of nodes in the mediastinum (cough and dyspnea) or on a nerve (pain).

TABLE 8.—*Atypical Lymphatic Leukemia*

[Mechanism: Chronic Lymphatic Leukemia Without Lymphemia]
Clinical types:
Only one type observed; clinically often confused with Hodgkin's disease; pathologically often confused with lymphosarcoma
Diagnosis:
1. Clinical:
A. Generalized adenopathy, often massive, and splenomegaly with apparently good health
B. No fever or weight loss
C. Urticarial or patchy erythematous rash at some time in course of disease
2. Hematologic:
Blood picture.—Usually normal; occasional eosinophilia; close scrutiny of lymphocytes reveals qualitative changes in these cells
Bone marrow.—Aspiration reveals variable lymphoid content; when over 25 per cent, confirmative
3. Biopsy:
Usually diagnostic; identical with lymphatic leukemia; occasionally histology of "follicular lymphoblastoma"

A summarization of the chief diagnostic facts in cases of "chronic" lymphatic leukemia when lymphemia is not apparent.

My experience indicates that an erythematous, patchy, sometimes macular, sometimes papular and occasionally typically urticarial pruritic rash on the skin is especially common in this type of lymphatic leukemia. This type of cutaneous lesion occurs commonly also in lymphatic leukemia with lymphemia [22] and is entirely unlike that seen in monocytic leukemia or Hodgkin's disease.[23] The chief points of aid in the recognition of this type of leukemia are listed in table 8.

CONCLUSIONS

1. A working hypothesis of the mechanisms responsible for the production of lymphatic leukemia includes two that are entirely dissimilar; one is neoplastic in origin, the other is neither neoplastic nor infectious in origin but possibly metabolic. Both types occur with and without lymphemia.

2. Disorder in nomenclature, failure to recognize the identity of the lymphocyte as a separate, distinct strain of cell and confusion of the diseases primarily involving the reticuloendothelial system with the diseases primarily involving the lymphocyte have militated against and have largely prevented a rational approach to an understanding of the lymphocyte and lymphatic dyscrasias.

3. There is evidence that there are only two basic primary noninfectious diseases of the lymphocyte. Both are potentially and always in some phase of the disease accompanied by quantitative and/or qualitative changes in the lymphocytes in the peripheral blood, although the mechanism of production of each is different.

4. This concept of the primary diseases of the lymphocyte, entirely aside from the supporting scientific evidence described, works in clinical practice, permitting accurate diagnosis, acceptable prognosis and maximum efficiency of treatment.

5. Finally, it is suggested, as the result of ten years of research and experience in this field, that correct diagnosis of the lymphatic dyscrasias can be achieved in a maximum number of cases only by the clinician-hematologist, who must consider, in the aggregate, the clinical features, peripheral blood, bone marrow and microscopic condition of the lymphatic tissue before a decision as to diagnosis can be given. The pathologist's interpretation of the lymph node alone often does not suffice. This is applying to the lymph node diseases a principle that has been established as valid through experience in the remainder of the blood dyscrasias.

22. Gates, Olive: Cutaneous Tumors in Leukemia and Lymphoma, Arch. Dermat. & Syph. **37**: 1015 (June) 1938.
23. Mercer, S. T.: Dermatosis of Monocytic Leukemia, Arch. Derm. & Syph. **31**: 615 (May) 1935.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. BETHELL AND WISEMAN

DR. RUSSELL L. HADEN, Cleveland: No disease puzzles me more or presents a more bizarre clinical picture than leukemia. It is a complex problem. The patient with unexplained fever and unexplained anemia must always have leukemia considered as a possible cause of his disease. Even after the diagnosis of leukemia has been correctly made, it often is impossible to be sure about the type. Dr. Bethell, after further study, has had to revise the original diagnosis in 10 per cent of the cases. The frequency of leukemia without leukocytosis should be emphasized. Dr. Bethell calls this the subleukemic form and Dr. Wiseman the atypical form of leukemia. Dr. Bethell told me this morning that 20 per cent of his series of patients are subleukemic. About 25 per cent of our patients with leukemia of all types never show a leukocytosis. The leukemia may be just as malignant with 2,000 as with 200,000 cells. My associates and I have been helped greatly in making the diagnosis of leukemia in the absence of leukocytosis by a careful study of concentrated preparations of the white cells. Dr. Bethell has emphasized the great variety of symptoms encountered in leukemia. The patient may have almost any symptoms since the disease is so widespread, although fever and anemia are by far the most common. Only 10 per cent of Dr. Bethell's group of patients with acute lymphoblastic leukemia had any enlargement of the spleen and lymph glands. The outlook for treatment in acute lymphoblastic and the lymphosarcoma cell types of leukemia is very poor. Perhaps the patients are much better off if nothing is attempted. I am impressed with the important place of arsenic in the treatment of chronic leukemia. I prefer to use it in combination with iodine. Many patients with chronic lymphatic leukemia judiciously treated with irradiation and arsenic will get along exceedingly satisfactorily often for years.

DR. SHIELDS WARREN, Boston: In the discussion of leukemia this morning, one thing has stood out more than anything else: our relative ignorance of the disease in spite of all the attention that has been focused on it. As brought out by Drs. Bethell and Wiseman, I believe this ignorance has been due partly to a onesided type of study. I am glad to hear them emphasize the need for consideration not only of the blood findings but of the clinical findings, also taking into consideration the micro-

scopic appearance of the lymph nodes and in the bone marrow as shown by biopsy. As a pathologist who has studied cases of chronic lymphatic leukemia at autopsy I cannot entirely agree with Dr. Wiseman in considering it as not a neoplastic disease. The extent of infiltration of the various viscera in the cases which do come to autopsy make me feel that until we have strong evidence to the contrary it is best retained in the neoplastic group.

DR. RAPHAEL ISAACS, Chicago: I was aware of the fact that the subject of leukemia is complicated, but I see it is even more complicated than I thought. The present concept of lymphatic leukemia may be simplified if we consider that there are really three conditions. One is a hyperplasia, or overgrowth of cells of the lymph glands. The second is an overgrowth of cells of the spleen. The third is a neoplastic condition which we may call lymphosarcoma. The cells of the lymph glands have round nuclei. The cells of the spleen have oval or kidney shaped nuclei. In other words, the spleen is not a lymph gland. So we have two kinds of lymphatic leukemias so called, one in which there is an overgrowth of lymphocytes and one in which there is an overgrowth of cells in the spleen. There may be lymphocytes invading the spleen or there may be spleen cells invading the lymph glands, but they are two different diseases, and I think the outlook in the two is quite different. At present I agree with Dr. Wiseman that there is a possibility that the lymphatic leukemia is hyperplasia of lymphoid tissue and that lymphosarcoma is a neoplastic condition. Some conditions appear to be converted into the neoplastic type by roentgen treatment. In fact, most of the patients with lymphosarcoma who became leukemic received roentgen treatment before they became leukemic. A therapy which we found helpful was that if the patients eat about half a pound of liver every day their red blood cell count and hemoglobin content remain nearer normal for a longer period of time than otherwise. Liver extract will not have this effect, but there is something in whole liver which influences the red blood cell count and hemoglobin in chronic lymphatic leukemia.

DR. B. K. WISEMAN, Columbus, Ohio: I don't think it possible at present to convince every one that there are two fundamental types of leukemia, one neoplastic and one nonneoplastic. As in the case of pernicious anemia, this will probably require the added evidence of therapeutic control. When I first started in this field, I also thought that all types of leukemia were neoplastic and I think I was unduly swayed in my judgment because of the animal types of leukemia—laboratory leukemia. After careful study of this disease, taking into consideration the clinical course, the morphologic aspects of the cells involved, the type of pathologic change that occurs in the lymph nodes with certain laboratory indications, such as the micrometabolism and tissue culture characteristics of these cells, it became evident to me that the so-called chronic type of lymphatic leukemia did not seem to possess many of the recognized traits of neoplasms in general. I think the leukemia of the laboratory animals is represented in the human field by the acute lymphatic type which does show neoplastic traits. This is also termed "lymphosarcoma cell leukemia" or "leukosarcoma." I think this concept makes quite clear any lack of conflict between the established facts of animal leukemia and those of human leukemia. I don't think "chronic" lymphatic leukemia is ever found in laboratory animals. Dr. Warren, of course, has all the data I presented in my written paper in support of the nonneoplastic hypothesis of chronic lymphatic leukemia. Time does not permit a satisfactory rebuttal based on factual evidence, but I listed these facts on the lantern slides although I didn't have time to emphasize them. Necessarily, I must be content to rest my case on the basis of the merits of the material developed in the written manuscript. With reference to Dr. Isaacs' remarks, I would say that I have not seen a chronic type of lymphatic leukemia which terminated in the lymphosarcoma type of leukemia. Assuming no inaccuracies in identification of cell types I would interpret this phenomenon as a coincidental occurrence of two separate disease states in the same individual. This would necessarily be an extremely rare occurrence.

CLINICAL VALUE OF THE ASCHHEIM-ZONDEK TEST IN THE DIAGNOSIS OF TESTICULAR TUMORS

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Since 1931 quantitative Aschheim-Zondek tests have been done routinely on patients with testicular tumors at Memorial Hospital. There have been 203 such patients, on whom a total of 1,403 urinary assays have been recorded. The tests were performed by the technic described by Ferguson in 1933. In addition there have been 42 on whom tests have been done with a larger number of animals per test in an attempt to make the assays more accurate. We wish to analyze data on these patients to answer the following questions:

1. Is the amount of hormone in the urine of a patient with a testicular tumor related to the histologic structure of the tumor?

2. Can one accurately follow the clinical course of the disease by repeated Aschheim-Zondek tests? Do these tests show increasing excretion of hormone, for instance, as evidence of recurrence or metastasis before such conditions can be discovered clinically?

3. Is the Aschheim-Zondek test as originally performed by us accurate, and if not why not?

4. Has the test any prognostic value in cases of testicular tumors?

5. Finally, is the test of sufficient clinical value to be worth doing? If it is, how should it be done?

Historically, the appearance of gonadotropic hormone in the urine of a man with teratoma testis was first observed by Zondek in 1929 [1] and reported, with a subsequent case, in March 1930. In September 1930 Heidrich, Fels and Mathias [2] published a detailed study of a case of chorioepithelioma of the testis, with data on the hormone in the urine. Ferguson's [3] first paper, based on a study of 12 cases, appeared in April 1931. The observation was made that irradiation caused a fall in the hormone output. In June 1933 Ferguson published a more extensive article,[4] reporting on a series of 117 consecutive testicular tumors studied by quantitative tests for gonadotropic hormone. From this material he came to the conclusion, reiterated several times in other articles,[5] that the histologic type of the tumor could be predicted by the amount of hormone excreted in the urine. For choriocarcinoma, 40,000 or more mouse units of prolan A per liter was given as characteristic; for embryonal adenocarcinoma, 10,000 to 40,000 mouse

From the Urological Service and the Oncological Laboratory of Memorial Hospital.

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1. Zondek, B.: Ueber die Hormone des Hypophysenvorderlappens: III. Follikelreifungshormon (Prolan A) und Tumoren, Klin. Wchnschr. **9**: 679-682, 1930.

2. Heidrich, L.; Fels, E., and Mathias, E.: Testikuläres Chorionepitheliom mit Gynäkomastie und mit einigen Schwangerschaftserscheinungen. Gleichzeitig ein Beitrag zur Pathologie der hormonalaktiven Gewächse, Beitr. z. klin. Chir. **150**: 349-384, 1930.

3. Ferguson, R. S.; Downes, H. R.; Ellis, E., and Nicholson, M. E.: Preliminary Note on a New Method of Differentiating the Testicular Tumors by Biological Means, Am. J. Cancer **15**: 835-843, 1931.

4. Ferguson, R. S.: Quantitative Behavior of Prolan A in Teratoma Testis, Am. J. Cancer **18**: 269-295, 1933.

5. Ferguson, R. S.: Studies in the Diagnosis and Treatment of Teratoma Testis, Am. J. Roentgenol. **31**: 356-365, 1934.

units; for embryonal carcinoma with lymphoid stroma, 2,000 to 10,000 units; for seminoma, 400 to 2,000 units, and for adult teratoma, 50 to 500 units.[5a] The statement that "the limits reached by each type of tumor overlap so little that it is possible to make the diagnosis on the basis of this determination alone" is found in an article published by Ferguson in March 1934.[6]

We have examined data in our files on 203 patients on whom satisfactory quantitative Aschheim-Zondek tests have been done to determine whether the foregoing statement is correct. For this purpose we limited ourselves to patients who had either an untreated primary tumor at the time of the first test or active untreated metastatic disease. Only 14 had tests of the urine done when a primary untreated testicular tumor was present and subsequently showed classifiable tumor tissue either on orchiectomy or biopsy of a metastasis or at autopsy. Thirty-six had urinary assays after the primary testicular tumor had been treated by irradiation or orchiectomy, with active untreated metastatic disease present when the assays were made.

For these reasons, therefore, only 50 patients of the 203 provided a suitable basis for answering the first question, regarding the correlation between the amount of hormone in the urine and the histologic structure of the tumor. The remaining patients fell into various classifications. For instance, some never showed any positive evidence of active disease while in this hospital, having come here for prophylactic irradiation. Others had been treated successfully here many years before the test was used and have remained clinically cured. Still others were given radiation therapy before a sample of urine was collected. Some refused orchiectomy, and no pathologic specimen was obtained. Some showed such complete destruction of the tumor by irradiation that no pathologic classification could be made.

Of the 50 tumors found suitable, 2 were adult teratoma, 3 were adult teratoma with areas of embryonal carcinoma, 4 were embryonal carcinoma, 20 were embryonal carcinoma with lymphoid stroma, 14 were embryonal adenocarcinoma and 7 were partially or completely choriocarcinoma. The last 7 may be further divided into 2 which were choriocarcinoma throughout, 2 which were embryonal adenocarcinoma with areas of choriocarcinoma and 3 which had areas said to be suggestive of choriocarcinoma. This classification appears in figure 1, in which it is also shown that the 2 patients in whom the tumor had strictly adult features excreted 0 to 500 mouse units per liter of urine. This was true also of 1 of the 3 patients in whom the tumor was adult and contained areas of embryonal carcinoma. The other 2 excreted 1,000 to 2,000 units per liter.

In the 4 cases of embryonal carcinoma there was no uniformity of hormone excretion, the amount ranging from 0 to 10,000 mouse units. The same lack of uniformity in hormone output was shown in the 20 cases of embryonal carcinoma with lymphoid stroma and in the 14 cases of embryonal adenocarcinoma. In general the more widespread the tumor the higher the hormone output; but this principle is not of much clinical use, because of frequent exceptions. For instance, there were 2 cases of embryonal carcinoma with lymphoid stroma and 3 of embryonal adenocarcinoma with extensive untreated metastatic disease in which only 100 to 500 mouse units was excreted per liter of urine.

In the 7 cases of either frank choriocarcinoma or areas suggesting it the excretion rate was high.

In the 50 suitable cases we made no attempt to revaluate the laboratory tests but merely used the figures as they had been placed on the charts. From the foregoing discussion it can be seen that there is no close relation in this material between histologic type and rate of hormone excretion. In general, however, when the tumor is of one of the less malignant adult types the excretion level tends to be low, while the choriocarcinoma causes the highest levels.

		HISTOLOGIC TYPE	NUMBER OF CASES		PROLAN-A (MOUSE UNITS PER LITER)	EXTENT OF DISEASE: LOCALIZED TO TESTICLE	MODERATELY ADVANCED	ADVANCED
1.	A	ADULT TERATOMA	5	2	0-500	••		
	B	ADULT TERATOMA WITH ISOLATED AREAS OF EMBRYONAL CARCINOMA		1	200	•		
				2	1000-2000	••		
2.		EMBRYONAL CARCINOMA (SOLID OR DIFFUSE) (SO-CALLED "SEMINOMA")	4	1	0		•	
				1	100-500			•
				1	5000			•
				1	10,000			•
3.		EMBRYONAL CARCINOMA WITH LYMPHOID STROMA (ALSO (SO-CALLED "SEMINOMA")	20	5	0-100	•	••••	
				5	200-500	•	••	••
				3	1000-1500		••	•
				6	2000-2500		•	•••••
				1	10,000+			•
4.		EMBRYONAL ADENO-CARCINOMA	14	1	0	•		
				5	100-500	•	•	•••
				5	1000-2500		•	••••
				3	10,000			•••
5.	A	CHORIOCARCINOMA	7	4	10,000+			••••
	B	EMBRYONAL CARCINOMA WITH AREAS SUGGESTING CHORIOCARCINOMA		2	1000-2000	•	•	
				1	10,000			•

Fig. 1.—Data on 50 cases of teratoma testis in which quantitative Aschheim-Zondek tests were done on the urine when active untreated disease was present. The amount of hormone excreted and the clinical extent of the disease are shown.

As mentioned previously, 42 cases have been studied in a more intensive fashion, with more mice per level than were used in the earlier tests. Of these 42, 19 are suitable for analysis. The remaining 23 are made up of 8 in which there were nonmalignant testicular swellings, 2 in which pathologic examination was not done, 8 in which there was no evidence of active disease at the time of the first test or subsequently and 5 in which the pathologic reports were unsatisfactory (because of destruction of the tumor or some other reason).

Among the 19 patients were 2 with choriocarcinoma. One of these excreted 200,000 mouse units per liter of

5a. By prolan A is meant a gonadotropin hormone which causes follicle ripening. No distinction was made between hormones of pituitary and those of placental origin.

6. Ferguson, R. S.: Clinical Evaluation of the Quantitative Excretion of Prolan A in Teratoma Testis, J. Urol. **31**: 397-409, 1934.

urine, and the other only 100 to 150. Among 11 with embryonal adenocarcinoma 1 excreted 64,000 mouse units per liter; 1, 40,000; 1, 5,000; 4, 2,000; 1, 400, and 3, 100 or less. All these patients had extensive metastases except the man excreting 40,000 units and the 1 excreting 400 units per liter. The first patient had a tumor in a testicle only. The second had a few metastases.

Among 5 patients with embryonal carcinoma with lymphoid stroma or seminoma there was 1 who excreted 20,000 units, 1 who excreted 1,000 and 3 who excreted less than 200 units. All 5 had fairly extensive metastases.

One patient with myosarcoma with metastasis excreted 400 units per liter.

In answer to question 1, then, our experience is that there is no definite correlation between hormone level and histologic appearance of the tumor. One cannot make the diagnosis seminoma, embryonal adenocarcinoma or even choriocarcinoma from data on the hormone excretion alone.

This is hardly surprising when one considers the histologic complexity of many of these tumors. Tumors classified as embryonal adenocarcinoma may show areas of complex teratoma, with various types of tissue, derived from other germ layers, present. Ferguson[7] himself, after study of 80 testicular tumors by large serial sections through the entire tumor, concluded:

> The malignant tumors of the testis are the result of neoplastic growth of the germ cell, and because this cell under certain circumstances (age, location, hormonal condition of the host) may exhibit but one or all of its potencies, these tumors are in a strict sense, teratoid in origin.

He mentioned a specimen in which chorioepithelioma, embryonal adenocarcinoma and seminoma were found in adjacent areas.

The tumor of the patient with embryonal carcinoma with lymphoid stroma in our last series who excreted 20,000 units per liter was typical in the first slide examined but in another area showed epithelial-lined cysts. Since most of the diagnoses used in answering our first question were made from small blocks of tumor, it is easily understandable that more complete examination of the entire tumor or of the metastases, were this possible, might give a different impression.

Can one follow the clinical course of the disease by repeated Aschheim-Zondek tests and predict metastases before they are clinically evident?

In answering this question we have relied chiefly on the 203 cases originally studied. Of the 203, 48 were not suitable, either because not enough information as to the clinical course was available or because only one assay was done.

In 74 cases no test yielded a level above 500 mouse units per liter; these cases are not considered, because consistently low levels cannot be used to affirm or deny the supposition that the excretion level follows the clinical course of the disease.[8]

In 47 cases there seemed to be close correlation between hormone levels and clinical course. In many of these there were consistently high levels of hormone which corresponded with clinical progress to a fatal outcome. In others a fall of hormone output appeared with intensive treatment and a rise with the appearance of metastasis.

In 34 cases, on the other hand, either rising hormone levels were not associated with progress of the disease or falling levels accompanied progressive cancer. Possibly the former occurrence may be explained by an increase in the excretion of pituitary gonadotropic hormone known to follow castration.

Obviously, a test which in only 47 of 155 serial determinations shows close correspondence with the condition of the patient is of little clinical value. Is it possible to find any reasons for this failure of correlation? It would seem reasonable to suppose that when a tumor produces a measurable amount of hormone increased growth will be accompanied by increased hormone output, and vice versa. That this was true in some of the 47 cases suggests that the exceptions must have an easy explanation.

In the technic devised and advocated by Ferguson and used in this laboratory until three years ago, 6 mice were used for each test. Five injections of a different amount of fresh morning urine or varying quantities of a 5 × alcoholic concentrate of this urine were given each mouse in two days. That is, only 1 mouse was used to determine the response at each of six different levels. When the animals were killed one hundred hours after the first injection, the final values were obtained by considering the formation of follicles in the ovaries as constituting a positive reaction. Thus if the mouse which received five injections of 0.2 cc. (1 cc.) of fresh urine showed follicle formation, it would be recorded that 1 mouse unit of hormone was present in 1 cc. of urine, or 1,000 units in a liter. If corpora lutea appeared, Ferguson multiplied by five the values obtained by the foregoing method, since Zondek had shown that it took approximately five times the amount of the urine of pregnancy to cause the formation of corpora lutea that it did to produce the ripening of follicles.

This method contains at least four sources of error:

1. Laboratory animals are so variable in their reactions to biologic products that to rely on only 1 animal per level is hazardous. This is shown by a study of the 42 cases in which 5 mice were used for each similar quantity of urine injected. In these cases, 430 tests were made on 2,150 mice. Of the 430 tests, 118 revealed the formation of corpora lutea or corpora haemorrhagica in the ovaries of at least 1 of the 5 mice. In other words, gonadotropic hormone appeared to be present. Yet in only 43 of these 118 tests were positive results obtained on all 5 mice. In 26 tests 4 of 5 mice showed corpora lutea; in 14, 3 of 5; in 18, 2 of 5, and in 17, 1 of 5; yet it is obvious that hormone must have been present to cause the formation of corpora lutea in even the last group.

2. To use a first morning specimen and calculate amounts of hormone per liter introduces variable factors such as the efficiency of the patient's kidneys and bladder and the amount of fluid he consumed the previous evening. A man with a daily output of 3,000 cc. of urine will not show the same amount of hormone per liter as one putting out exactly the same total quantity in 1,000 cc. A patient whom we studied carefully with serial daily hormone determinations suddenly increased his output of urine from 1 liter to 5 while under observation, explaining when questioned that he thought it was "a good thing to drink plenty of water." Only twenty-four hour collections are rational in such a metabolic study and, as a matter of fact, well preserved three day collections would probably give even more accurate results.

7. Ferguson, R. S.: Teratoma Testis: Pathogenesis of the Malignant Tumors of the Testis, Preliminary Note, Cancer Probl., Symposium, 1937, pp. 86-91.

8. Variations from 100 to 500 units probably are meaningless with the technic that was used.

3. To make a 5 × concentration of urine by precipitation with 95 per cent ethyl alcohol is to invite error. Alcoholic precipitation appears to be among the most satisfactory procedures for concentrating and recovering gonadotropic hormone, but the amount so recovered is highly variable. We have had the experience of finding no hormone in an alcoholic extract of a specimen of urine which showed appreciable amounts when unconcentrated. By the statement that this process invites error we do not mean to deny the value of concentrating urine by alcoholic precipitation but wish to point out the fallacy of supposing that such a procedure gives 100 per cent recovery of hormone.

4. To take as an end point the formation of follicles in the ovary and to assume that five times the amount of hormone which causes this result will produce corpora lutea is wrong. At least two gonadotropic hormones now are known to occur in urine. These are the follicle-stimulating hormone from the pituitary, found in one or two of the many follicles present show development. It is necessary, then, to record values in levels of chorionic gonadotropic hormone and follicle-stimulating hormone separately and to control one's observations by microscopic section of the ovaries of the experimental animals.

If we have shown that the quantitative Aschheim-Zondek test as it can be carried out practically has little value in disclosing the type of the testicular tumor or in accurately following the clinical course of the disease, is it of any clinical value? We believe that this question should be answered in the affirmative, because our records show that the appearance of chorionic gonadotropic hormone is a bad prognostic sign. Of the original 203 patients with testicular tumor studied, those who showed a hormone level which never went above 1,000 mouse units per liter had a mortality of 33 per cent. This means that, of all patients tested from 1931 to 1939, 77 per cent were alive in July 1939.

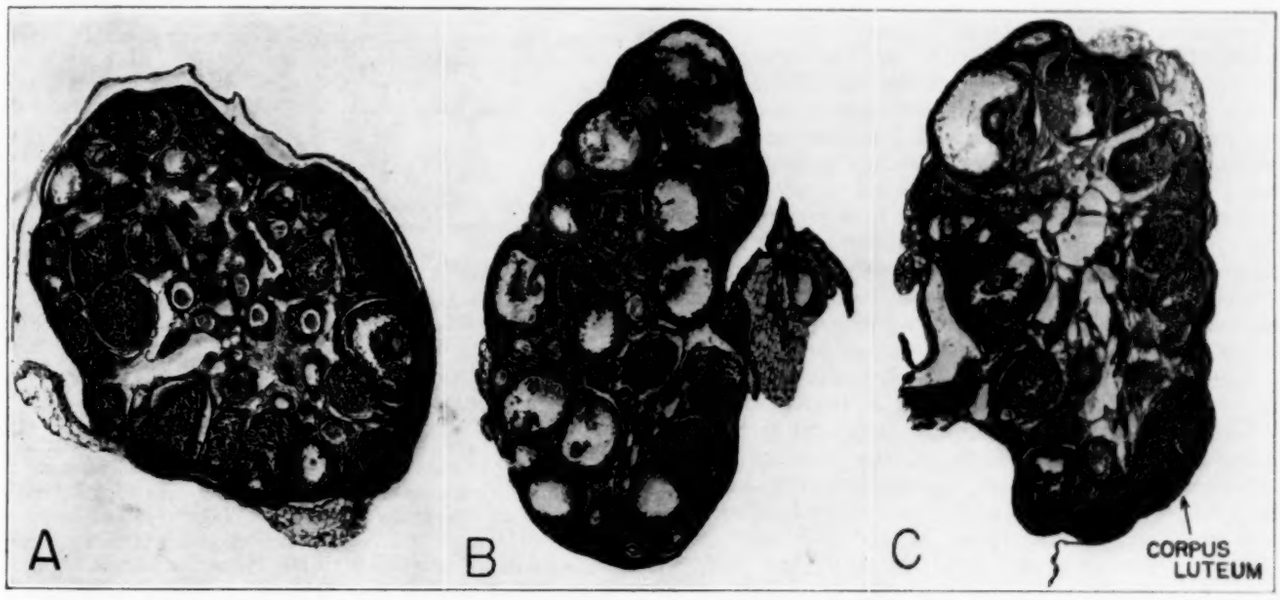


Fig. 2.—*A*, ovary of a mouse inoculated with urine from a patient showing no gonadotropic hormone. *B*, ovary of a mouse inoculated with urine from a castrate. Note that nearly all follicles show ripening but no corpora lutea are present. This effect is due to the presence of follicle-stimulating hormones, probably from the anterior lobe of the pituitary gland. *C*, ovary of a mouse inoculated with urine from a patient with active teratoma testis. Note that there is only one ripe follicle at the top of the section but a corpus luteum at the bottom. This effect is due to the presence of chorionic gonadotropic hormone.

large amounts in the urine of male and female castrates and of women past the menopause, and the chorionic gonadotropic hormone of the urine of pregnancy (fig. 2). The latter causes luteinization of follicles already formed, and in the hypophysectomized rat the effect is one of luteinization of interstitial cells. The action of the follicle-stimulating hormone is primarily the formation of follicles. Both hormones are found in the urine of patients with teratoma; occasionally they may be present together, but it is likely that one may predominate over the other. A patient studied by us repeatedly had positive reactions at 1,000 to 2,000 mouse units per liter though clinically free of disease. Microscopic study of the assay mouse ovaries showed ripening of all visible follicles, with either no corpus luteum or only an occasional one. The positive reaction was a castration effect. On the other hand, specimens of urine may give rise to many corpora lutea and few ripe follicles. Diluting such urine does not result in the picture of profuse maturation of follicles described but rather produces a condition of the ovary in which only

If a patient excreted 1,000 to 2,000 mouse units of hormone per liter he belonged to a group of which 57 per cent were dead on that date. Those excreting 2,500 mouse units or more per liter showed an 82 per cent mortality.

Thirty patients were recorded as excreting 10,000 mouse units or more per liter. All who showed this amount on more than one occasion are dead.

Of the 42 patients studied more carefully for level of excretion and type of hormone, the urine of 18 in some dilution gave rise to corpora lutea of the pregnancy type in the ovaries of the test animals. Of the 18, 14 died in less than three years, while 1 is still living but has extensive metastatic disease. The 3 patients apparently cured are 1 whose highest output was 200 mouse units per day of what appeared to be chorionic gonadotropic hormone, a second whose urine showed in a single test 10,000 mouse units of this type of hormone until removal of the tumor, after which it showed only small amounts of follicle-stimulating hormone, and a third with metastatic seminoma, whose urine never

produced corpora lutea but did produce follicle ripening, suggesting the presence of chorionic gonadotropic hormone, excreted in amounts of 100 units every twenty-four hours.

Of 16 patients whose urine showed small amounts of what appeared to be follicle-stimulating hormone or no hormone at all, 13 are living and apparently free of disease, while 3 have died. We have been unable to confirm the suggestion of Hamburger[9] that follicle-stimulating hormone is found in the urine of patients with seminoma (for him a term including embryonal carcinoma and embryonal carcinoma with lymphoid stroma) and chorionic gonadotropic hormone in that of patients with adenocarcinoma or chorioma. Both types of hormone are found in each group of patients, we believe.

Finally, from the clinical point of view is the Aschheim-Zondek test worth doing in all cases, and if so how should it be done? We believe that the test is valuable, since positive results are of grave prognostic value and not infrequently constitute the only evidence of disease. An example of this is a recent case in which the diagnosis originally was tuberculous epididymitis on the left. Two tests were done on the urine before any treatment was begun, and each revealed a considerable quantity of chorionic gonadotropic hormone. On the basis of these tests a diagnosis of teratoma testis was made, and it proved to be correct on orchiectomy. After operation and roentgen therapy the test continued to give positive results, though there was no clinical or roentgenologic evidence of disease. Eleven months after operation, there being increasing excretion of hormone in the urine, metastatic disease in the mediastinum was finally found by roentgenogram.

We believe that the test can be satisfactorily performed in the following manner: A twenty-four hour collection of urine should be assayed on 6 mice as recommended by Ferguson. If any react positively, quantitative determinations should be performed. At least 5 mice should be used for each assay level and the ovaries of all animals should be studied histologically. Uniform ripening of follicles, suggesting the pituitary type of hormone (follicle-stimulating hormone) seems to be of little prognostic significance. The formation of corpora lutea, especially of the chorionic hormone type, is important. A negative reaction is of little clinical significance because considerable disease may be present. A strongly positive reaction of the chorionic type is highly important because, according to our experience, it signifies active disease and usually a fatal prognosis.

SUMMARY

1. A study of 203 cases of testicular tumor in which quantitative Aschheim-Zondek tests were done by the method of Ferguson and a study of 42 cases in greater detail, with a larger number of mice per assay level, revealed little correlation between the amount of gonadotropic hormone found in the urine and the histologic type of the tumor.

2. In only 47 of 155 cases in the series followed by serial tests done by Ferguson's technic was there any close correlation between the hormone level and the clinical course of the disease.

3. The failures in correlation may be ascribed to the inadequacy of the test as originally described.

4. The presence of chorionic gonadotropic hormone in the urine means that there is an active tumor somewhere in the patient and suggests a bad prognosis. Eighty-two per cent of the patients whose urine showed 2,500 or more mouse units per liter are dead. All patients who excreted 10,000 mouse units per liter more than once are dead. In the test as used, "10,000 mouse units" indicates the presence of chorionic gonadotropic hormone.

5. By suggestions given for doing the quantitative Aschheim-Zondek test, a number of errors in the former technic may be corrected.

York Avenue at Sixty-Eighth Street.

9. Hamburger, C.; Bang, F., and Nielsen, J.: Studies on Gonadotropic Hormones in Cases of Testicular Tumors: Attempt at Classification of Testicular Tumors on the Basis of Their Hormonal, Histological, and Clinic-Radiological Properties, Acta path. et microbiol. Scandinav. **13**: 75-102, 1936.

ABSTRACT OF DISCUSSION

DR. JOSEPH H. KIEFER, Chicago: We do not see nearly so large a number of cases in Dr. McKenna's service at the Research and Educational Hospitals of the University of Illinois, but in the last four years we have determined the gonadotropic hormone output in every one. The Zondek alcohol precipitation method has been used routinely. This gives a set of values which differs considerably from that obtained when unaltered urine is used. In some cases, in which we made parallel determinations with both extract and unaltered urine, a ratio of approximately 3 to 1 was found to exist. Some of the earlier reports proposed that one could determine the type of tumor present by the titer of the hormone output. Also it was said that one could determine the presence of metastases with assurance and regulate roentgen therapy accordingly. Some authors even proposed a classification of these tumors in which the primary standard of division would be hormone output, and the secondary divisions into subgroups would be made according to the histologic picture. A few reports have appeared since in which the value of this method has been denied. We have found that routine use of this test has been useful in diagnosis. We have found no positives in nonmalignant lesions. Several of these cases were so suggestive as to warrant surgery despite the negative hormone output. In every case the lesion has proved to be nonmalignant. We have so far had no case of tumor in which a preoperative determination was negative. We have not been able to correlate the histologic type and hormone output in any more than a very inexact way. Likewise extent of metastasis did not give a corresponding increase in hormone output. Some patients with extensive demonstrable metastases showed only minimal hormone outputs. Some others, apparently well after orchiectomy and roentgen therapy, continued to show these same low values for years (possibly a castration effect). Hormone determination is a valuable aid to diagnosis and, with definite restrictions, in prognosis. Possibly with further knowledge as to the exact nature of the hormone formed, tests of this nature will take on added value. In many cases gonadotropic hormone may be only one of several hormones elaborated by these growths. If these totipotent cells can elaborate gonadotropic hormone, why not estrogens and others? How else can one explain gynecomastia with colostrum formation? Some investigators have found estrogen excretion in these cases.

DR. J. B. GILBERT, Schenectady, N. Y.: It is important to remember that frequently the original technic is the best, and modifications often increase the difficulties of its proper application. This test must be done in great detail, which allows no short cuts. This detailed and expensive work is often possible only in research institutions. From the practical standpoint in the vast majority of patients as seen by urologists in smaller hospitals the procuring of exact quantitative tests is frequently impracticable or often actually impossible. The test as used in most hospitals is poorly standardized, as some use mice, others rats, and many rely on a single intravenous rabbit injection. A summary of the results and the true importance of such tests is almost impossible to determine by reference to the collected urologic literature. The correlation between hormone levels and pathologic type is extremely difficult because of possible errors in both the microscopic examination of tissue and the aforementioned errors in endocrine methods. Confusion in this

subject has been caused by misdefinition and inexact terminology. This confusion arose in Aschheim-Zondek's original description of reactions I, II and III and was later increased by the use of the terms "prolan A and B." The fact that the origin of the so-called prolans is not known for certainty makes an exact definition difficult, if not impossible. The authors' use of the term "chorionic gonadotropic hormone" is useful and should be followed by others. The fact that the finding of such a hormone, with corpus luteum formation in the ovaries, indicates a bad prognosis is extremely important. This was found to hold true in our study of personal and collected cases in which testis tumors were associated with gynecomastia, also in another series of small obscure primary testis tumors in which hormone assays aided in the early diagnosis and prognosis in 21 of 53 cases. The clinical course when based on histologic grading has been inexact, and only to a moderate degree have the hormonal tests clarified this situation. The authors do point out, however, that a roughly useful working guide to prognosis and therapy can be obtained; also that at least positive findings are important and may constitute the only evidence of disease. Together with the aid of these tests and the expert knowledge gained from treatment of many patients, the survival rate in their hands at the Memorial Hospital is unusually large. A 14 per cent survival in inoperable testis cancer treated under these conditions is proof of their careful and intelligent clinical management and valuable aid received from the laboratory.

DR. GRAYSON CARROLL, St. Louis: The authors speak of orchiectomy. Do they attempt to remove the retroperitoneal lymph glands in their operative procedure or have they abandoned that? I am aware that in most of the textbooks it indicates that that should be done whenever possible.

DR. GRAY H. TWOMBLY, New York: Dr. Kiefer's report differs from ours in that he seemed to find positive hormone tests in all his cases. I could mention a dozen cases in our clinic in which there was a testicular tumor present, but no hormone. I wonder whether he made any study of what type of hormone was present. It is possible the tumor itself growing in the testis and destroying it may influence the pituitary to secrete the castrate type of hormone. Our experience is that only a positive test is of diagnostic value and a negative test means nothing. I have seen a case in which the lungs were filled with metastases that had an absolutely negative test as far as we could determine. He said something about estrogens in these cases. We ran estrogenic determinations on one man who had a chorioepithelioma of the testis with gynecomastia. He had a titer which was about twice as high as that of the normal female and, of course, a great deal higher than that of the normal man. But I don't believe that much estrogen is excreted in most cases of teratoma testis. Dr. Gilbert was complimentary about our handling of these tumors. I didn't quite like his saying he felt that the test was not practical. I feel that the study we have made really makes the test more practical than it was before, because it appears that repeated tests to try to follow the course of the disease are not worth while doing in most cases but that the test in which we try to find out whether the patient is excreting chorionic gonadotropic hormone or not is tremendously worth while. All the people that really excreted it in large amounts died of the disease. He brought out the variability in microscopic appearance of teratoma. There can be a choriomatous tissue in one part of the tumor, seminoma in another part, adult type of tumor in another part, embryonal adenocarcinoma in another part. In answer to Dr. Carroll's question it has been the policy at Memorial Hospital to do the orchiectomy only after the roentgen therapy. However, it seems to me that, if one exposes the cord and ligates it carefully, one cuts off all the lymphatics. There isn't any possibility of spread taking place up the cord while one is manipulating the testis, if one has already cut the lymphatic channels. Then the tumor can be lifted out of the scrotum, giving a gross specimen that one can really study properly in the laboratory, both pathologically and from the hormone point of view. It has been the feeling of the men in the urologic department that wide dissection of the nodes in the iliac region, as Dr. Hinman does, is a procedure that does not give a high enough cure rate to justify the risk to the patient in that procedure. The routine treatment has been to treat the testis and then the iliac and epigastric regions with large amounts of roentgen ray.

THE TECHNIC OF BRONCHOGRAPHY AND A SYSTEM OF BRONCHIAL NOMENCLATURE

RALPH ADAMS, M.D.
AND
LOWREY F. DAVENPORT, M.D.
BOSTON

As refinements in the technic of pulmonary resection have lowered mortality and morbidity rates, the medical profession and the group of patients symptomatically concerned have become increasingly interested in the possibility of relief from cough or sputum and the number of cases requiring critical evaluation has risen sharply.

Bronchography, as roentgen demonstration of the bronchial pattern by opaque mediums is called, is an essential diagnostic aid in the investigation of many such patients, and the use of the procedure has become widespread during recent years. Commendable as is the enthusiastic study of patients with a cough by all measures likely to discover its cause, the general use of iodized oil injection has raised certain problems. Numerous patients have been seen in consultation in whom a diagnosis of bronchiectasis has been established elsewhere by demonstrating iodized oil filling one or more grossly dilated bronchi in one or more lower lobes. The filling is adequate for substantiating a diagnosis of bronchiectasis but inadequate for a basis on which to plan a surgical program, and the patient must be requested to undergo another injection. Oftentimes objections are encountered because the initial procedure is recalled as a nightmare, attended by violent coughing, nausea, vomiting, excitement and general confusion. Patients sometimes also are inquisitive as to why the original injection was not done in such a manner as to give the information required.

We have done several hundred iodized oil injections in the past seven years by various methods [1] and have developed a simple, proved technic which is almost uniformly successful and is suitable for use by any physician willing to learn a few principles and respect scrupulously the details of application. The time has come when an accurate, complete, intelligently made bronchogram can reasonably be expected of any one who undertakes the procedure. No longer is it sufficient to succeed in getting a few drops of iodized oil into some part of the tracheobronchial tree; on the contrary, every bronchial segment should be visualized in order that the extent of the disease may be established and a proper plan of therapy instituted. Especially is this important if surgery is indicated, because decision concerning the amount of lung tissue to be resected must rest largely on the bronchogram.

TECHNIC

The technic requires simple materials, and no special equipment is needed. Adequate facilities for making good x-ray films of the chest are assumed. The materials required are:

(*a*) Two chairs, a small work table, an adjustable electric light and a flat-top table.

From the Thoracic Clinic of the Massachusetts General Hospital.
Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Goldman, Alfred, and Adams, Ralph: Endobronchial Probing Combined with Serial Selective Bronchography Fluoroscopically Controlled, Ann. Surg. **106**: 976 (Dec.) 1937.

(*b*) A head mirror, a laryngeal mirror, an atomizer, 6 inch cross forceps, small cotton or gauze pledgets, a 2 cc. syringe and curved applicator, an ordinary number 16 urethral catheter and stylet and a 20 cc. syringe (fig. 1).

(*c*) A 5 cc. measuring flask, two 5 cc. glass containers, 4 per cent cocaine, 5 per cent larocaine and 20 cc. of iodized oil.

PRELIMINARIES AND ANESTHESIA

Preoperative medication is not essential but is beneficial in achieving abolition of cough, a suppression of mucous membrane secretions and proper introduction of oil. A small dose of pentobarbital one hour beforehand helps allay nervousness and acts as a specific prophylactic antidote to cocaine hypersensitivity. In our hands the preliminary medication with pentobarbital has prevented severe cocaine reactions. These most often occur in apprehensive persons of the sympatheticotonic type. The initial reaction is largely due to the vasomotor effect and can be promptly relieved by the inhalation of amyl nitrite. A dose of morphine sulfate one-half hour beforehand is useful for its effect in controlling the cough reflex. Atropine, given with the morphine, decreases the amount of secretion and thereby enhances the efficiency of topical anesthesia and iodized oil distribution.

Fig. 1.—Materials required.

It is important to have the bronchi empty at the time of examination. Postural drainage accompanied by voluntary coughing and efforts to raise sputum three hours before injection is used to this end. Thereafter the patient should neither eat nor drink until three hours after the procedure. Unless the bronchi are cleared of secretion before the injection, the examination will be rendered unsatisfactory by spasmodic coughing due to poor anesthesia and by failure of iodized oil properly to enter and delineate secretion-filled areas. The oil should be introduced and the x-ray films taken in the same room. The induction of anesthesia and the introduction of a catheter can be done in an adjoining room if this procedure is desirable, but the patient should not be made to walk from one room to another after the oil has been injected, as loss of time or involuntary cough will cause the picture to be marred by alveolar filling.

A sitting position should be used for the induction of local anesthesia to the throat and tracheobronchial tree. The physician should sit opposite with the small work table and materials at his right and a light behind the patient's shoulder. Good anesthesia is prerequisite to good bronchography. This statement cannot be overemphasized, and it can be stated with almost equal truth that poor bronchography is due mainly to poor anesthesia. A large quantity of anesthetic is not desirable and, in fact, is contraindicated. Proper topical application of 10 cc. of 4 per cent cocaine hydrochloride solution or 5 cc. of 4 per cent cocaine and 5 cc. of larocaine gives an excellent preparation with abolition of the involuntary cough reflex. Our custom is to spray the pharynx with 3 cc. of 4 per cent cocaine, swab each piriform sinus and the epiglottis with 1 cc., and inject 5 cc. of 5 per cent larocaine down the trachea. Larocaine is used for intratracheal instillation because of its theoretical advantage of lowered toxicity in comparison with cocaine. No reaction has been encountered with either agent.

INSERTION OF CATHETER

The method used is similar to that described by Baker.[2] The urethral catheter is threaded on the metal stylet, bent to an 80 degree angle 3 inches from the distal end. The laryngeal mirror is used and the catheter is introduced into the trachea and the stylet removed. The catheter should lie about 2 inches above the carina, and no effort is made to introduce it into the primary bronchi. The patient closes his lips on the catheter and then is asked to sit on a flat top table adjacent to an x-ray tube stand, where the actual injection is done.

IODIZED OIL INJECTION

A series of positions is assumed as the injection proceeds which allows gravity filling of all bronchial subdivisions. These are outlined in the accompanying series of sketches. The side of the chest suspected of disease should be examined first. If both sides are under scrutiny, it is customary to fill the left side first. The iodized oil is injected at room temperature, as this minimizes alveolar filling.

Figure 2. Four cc. is run down the left primary bronchus into the dorsal divisional bronchus and the lower lobe segmental bronchi. The position is held for one minute.

Figure 3. Two cc. is run down the left primary bronchus and into the left upper lobe bronchus. The position is held for one-half minute.

Figure 4. One cc. is injected to insure filling of the lingula as it is brought into dependent position. After one-half minute 3 cc. is injected and the patient is placed in the position of figure 5.

Figure 5. The position is held for two minutes to fill the apical segments and the patient is turned into the position of figure 6.

Figure 6. This position is held for one minute to complete filling of the posterosuperior segment and the dorsal division and then changed to the position of figure 7.

2. Baker, D. C., Jr.: Pneumonography, Laryngoscope **46**: 873-877 (Nov.) 1936.

Figure 7. This position is held for one-half minute to insure complete filling of the basal division and then changed to the position of figure 8.

Figure 8. This position is held for one-half minute and a lateral view x-ray film is exposed with the patient lying on a cassette holder and the x-ray tube 4 feet above the table top.

At this point seven minutes will have elapsed and 10 cc. of iodized oil will have been injected. Filling

Figs. 2 to 10.—Positions held during injections of iodized oil.
Figure 2.

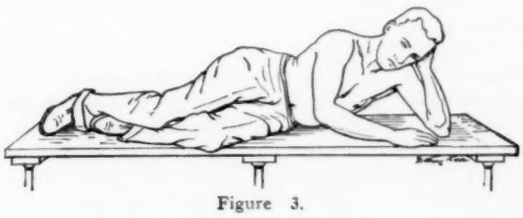


Figure 3.

Figure 4.

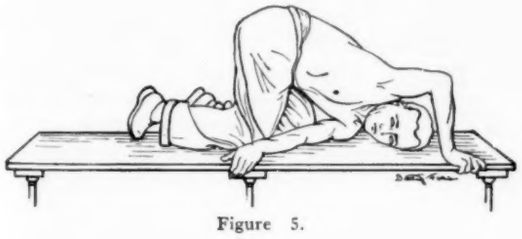


Figure 5.

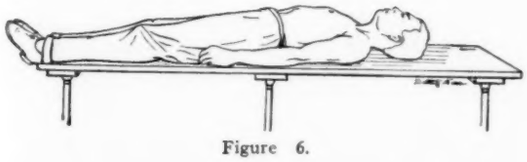


Figure 6.

of the opposite side is begun immediately and is performed in a manner similar to that just described. The right middle lobe will be filled by positioning comparable to that used for outlining the lingula on the left side. At the end of the procedure 20 cc. of iodized oil and fifteen minutes will have been required.

The patient then moves off the table and stands before an upright cassette 5 to 7 feet from the x-ray tube, where four additional exposures are made. These are:

(*a*) Posteroanterior.
(*b*) Posteroanterior with Lysohm grid.
(*c*) Right anterior oblique (fig. 9).
(*d*) Left anterior oblique (fig. 10).

These films are developed immediately and examined. Meanwhile the patient lies quietly on a table. If any exposures need to be repeated, that is done. If the

Figure 7.

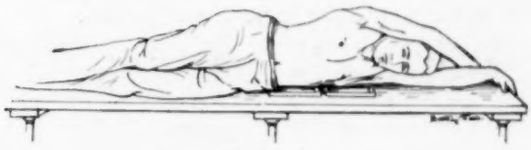


Figure 8.

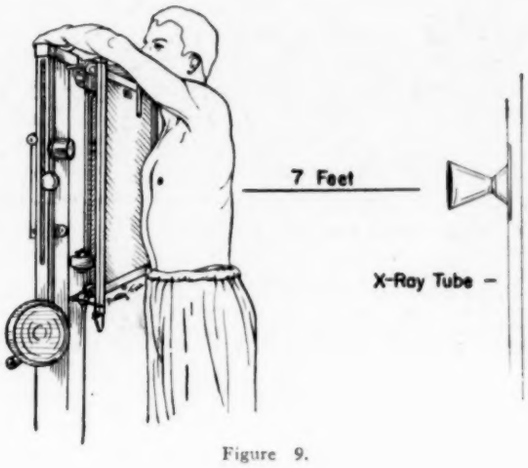


Figure 9.

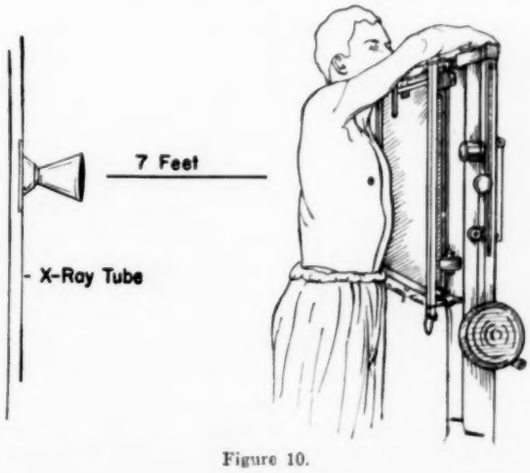


Figure 10.

films are found satisfactory, the patient is placed in the head-down position and urged to cough up the iodized oil.

DETAILS OF FILMS

Thin, over-all coating of the bronchi is preferable. Alveolar filling is to be avoided.

One good posteroanterior film will often give most of the information needed for diagnosis. The others are necessary for confirmation, for careful study of special segments and for assurance that necessary views for subsequent study will be available. One cannot reduce the number of films without risk of lacking essential information on an important case.

The first lateral film taken defines posterior and anterior branches of the suspected side and gives a picture of spatial relationships that cannot be had when both sides are filled because of overlying shadows. The grid film allows detailed study of areas that may be too dense to show in ordinary films, such as an atelectatic left lower lobe lying behind the heart. By means of the right anterior oblique position the left side is thrown forward into relief, presenting a view of the important lingula bronchus (fig. 9). A similar portrayal of the right middle lobe is accomplished with the left anterior oblique exposure (fig. 10).

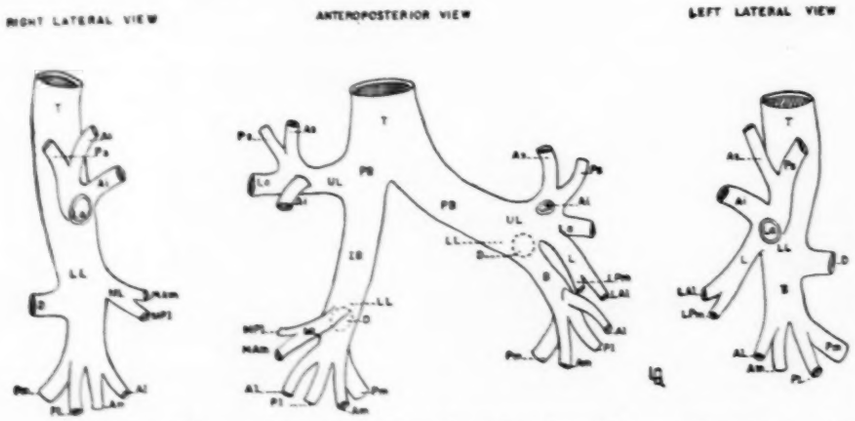


Fig. 11.—Bronchial tree: *T*, trachea; *PB*, primary bronchus; *UL*, upper lobe bronchus; *Ai*, anteroinferior segmental bronchus; *La*, lateral segmental bronchus; *As*, anterosuperior segmental bronchus; *Ps*, posterosuperior segmental bronchus; *D*, dorsal divisional segmental bronchus; *ML*, right middle lobe bronchus; *LL*, lower lobe bronchus; *Pm*, posteromedial segmental bronchus; *Am*, anteromedial segmental bronchus; *B*, basal divisional bronchus; *L*, lingula divisional bronchus; *Pl*, posterolateral segmental bronchus; *Al*, anterolateral segmental bronchus; *LAl*, anterolateral segmental bronchus of lingula; *LPm*, posteromedial segmental bronchus of lingula; *MPl*, posterolateral segmental bronchus of right middle lobe; *MAm*, anteromedial segmental bronchus of right middle lobe; *IB*, intermediate bronchus.

CONTRAINDICATIONS

Cases of active pulmonary tuberculosis, acute lung abscess, intrinsic asthma and suspected tumor should not be investigated by means of iodized oil unless exceptional reasons exist for the procedure. The information as recorded by iodized oil films frequently may be more striking in these cases but rarely is it additional to that available from x-ray study alone. Spread of tuberculous infection has been observed after iodized oil injection, and retained oil complicates indefinitely the interpretation of parenchymal shadows. Asthmatic persons occasionally suffer acute respiratory distress following injections, and care should be exercised to inject only one side if iodized oil films are deemed essential for study of localized disease. A diagnosis of obvious bronchial tumor may be more clearly demonstrated to the uninitiated by means of iodized oil, but important incipient signs may also be hidden from the expert in a difficult early case. Careful fluoroscopy and films in expiration as well as inspiration are more valuable aids in such cases. Oil trapped behind an obstructing tumor is a hazard that should be avoided, as it may cause pneumonitis.

NOMENCLATURE

The problem of correctly naming the tracheobronchial subdivisions has become increasingly pressing as technics of x-ray reading, bronchoscopy, bronchography and pulmonary resection have appeared and improved. A complete reexamination of the surgical anatomy of the subdividing pulmonary vessels and bronchi has been required with attention not only to details of structure but also to simplification and improvement in nomenclature in order to meet modern practical requirements. As early as 1889 Ewart,[3] stimulated by the original work of Aeby, published a classic monograph on "The Bronchi and Pulmonary Blood Vessels." The prefatory paragraph is of historical interest:

> These pages have a general purpose which extends beyond the limits announced in their title. They represent an attempt to remove the too prevalent impression that the field of pulmonary investigation, having yielded all its fruit, is henceforth likely to remain barren. Although advised, not long ago, by an eminent physician, to turn my attention to some other organ less "worked out" than the lung, I have found no reason to complain of my subject, and I may even succeed in showing that, so far from this being an exhausted territory, there remain within it some districts almost unexplored. . . . Moreover, a suspicion has arisen in my mind that the present deficiencies in our anatomical knowledge (some part of which it will be my endeavor to fill) might perhaps be held responsible for the halting and spasmodic feature in the development of pulmonary surgery, contrasting with the steady progress made in the surgery of other organs.

Ewart's monograph was the first serious attempt to construct a systematic nomenclature of the air tubes. He presumed the lack of a system due both to lack of need for one and to lack of systematic study. Since his time the need for a uniformly accepted system has increased steadily, and the bronchial distribution has been made a subject for intensive systematic study by numerous authors, much of it of a high order.[4] The present difficulty arises from a plethora of names for each ramification and from an effort to carry into working charts such details and variations as might more suitably be confined to the fundamental works of reference. Troubles have arisen, therefore, both from complexity of the individual systems and from lack of agreement among them.

3. Ewart, William: The Bronchi and Pulmonary Blood Vessels: Their Anatomy and Nomenclature, with a Criticism of Professor Aeby's Views on the Bronchial Tree of Mammalia and of Man, London, J. and A. Churchill, 1889.

4. Articles on bronchial distribution:
Sicard, J. A., and Forestier, Jacques: Méthode générale d'exploration radiologique, par l'huile iodée (lipiodol), Bull. et mém. Soc. méd. d. hôp. de Paris **1**: 463, 1922.
Bethune, N.: Technique of Bronchography for General Practitioner, Canad. M. A. J. **21**: 662 (Dec.) 1929.
Davis, J. D.: Anatomic Variations of Normal Tracheobronchial Tree, Arch. Otolaryng. **9**: 404 (April) 1929.
Kramer, R., and Glass, A.: Bronchoscopic Localization of Lung Abscess, Ann. Otol., Rhin. & Laryng. **41**: 1210 (Dec.) 1932.
Moolten, S. E.: Simple Apparatus for Fixation of Lungs in Inflated State, Arch. Path. **20**: 77 (July) 1935.
Levitin, Joseph, and Brunn, Harold: A Study of the Lower Lobe of the Lung, Arch. Int. Med. **57**: 649 (April) 1936.
Grandgérard, R., and Heim de Balsac, R.: La trame primaire des poumons et la destination corticale de ses ramifications; étude anatomique, radiologique et clinique, Presse méd. **45**: 444 (March 20) 1937.

(Footnote 4 continued on next page)

In the belief that a simple terminology, acceptable to a majority of workers in the thoracic field, is a primary condition for successful study and continued advance in the subject, we are proposing a classification designed to meet the practical needs of internists, radiologists, bronchologists and surgeons. It is in no sense a new arrangement and new names are not recommended, as our first concerns are simplification and reduction of confusion. Personal investigation of material at the operating table and of fresh autopsy specimens over a five year period has furnished first hand knowledge for the task of synthesizing the terminology of the proposed system.

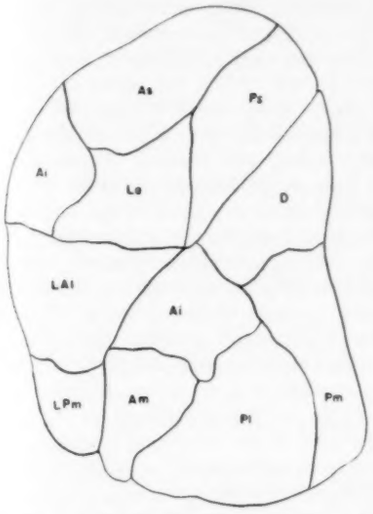


Fig. 12.—Left lung, lateral view: *As*, anterosuperior segment; *Ps*, posterosuperior segment; *Ai*, anteroinferior segment; *La*, lateral segment; *D*, dorsal divisional segment; *LAl*, anterolateral segment of lingula; *Ai*, anteroinferior segment; *LPm*, posteromedial segment of lingula; *Am*, anteromedial segment; *Pl*, posterolateral segment; *Pm*, posteromedial segment.

The clinical study of bronchopulmonary subdivisions is made on x-ray films taken after injection of iodized oil. These films necessarily record on a single plane the projection of bronchi into myriad planes. Schematic representation of the bronchial tree by free-hand drawings may wander far from reality when one relies for accuracy on artists' impressions of spatial relationships. Therefore the diagrams used here are actual tracings from actual bronchograms of patients under clinical investigation (fig. 11 and the table). The proposal specifically omits the finer ramifications and subdivisions, the practical importance of which from the standpoint of diagnosis and therapy lie in the future. Working terminology for these finer tubes may be added to the present system whenever the need arises.

The term primary bronchus is suggested for the two divisions of the trachea as preferable to main, major, arterial or trunk. The classification according to lobes is obvious and follows the usage of all authors except Nelson.[5]

The peripheral marking of the lungs by fissures and septums is subject to considerable irregularity and variation in degree. For example, the right middle lobe frequently is scarcely demarcated from the right upper lobe, while the dorsal division of the right lower lobe occasionally is separated by a distinct fissure from the basal division, and the lingular division of the left upper lobe shows wide variations in depth of fissures. These portions of the lung have special significance both pathologically and surgically. Pulmonary tuberculosis occurs predominantly in the apical division. The lingula is involved in bronchiectasis in 80 per cent of the left lower lobe cases.[6] The dorsal division of the lower lobe is a frequent site of putrid lung abscess. Involvement of this same division by bronchiectasis is rare, even though the predominant site of bronchiectasis is in the contiguous basal division of the lower lobe. The ability to remove these portions surgically for localized disease has been demonstrated. The term division is proposed to indicate these surgically and pathologically important anatomic portions of lobes. Thus, the left upper lobe has apical and lingular divisions and each lower lobe has dorsal and basal divisions. The right upper lobe may be thought of, if desired, as having only an apical division, while the right middle lobe possesses no divisional substructure.

Structural Anatomy of the Lung

Lobe	Division	Segment
Left upper	Apical	Anterosuperior Posterosuperior Lateral Anteroinferior
	Lingular	Anterolateral Posteromedial
Left lower	Dorsal	
	Basal	Anteromedial Posteromedial Anterolateral Posterolateral
Right upper	.....	Anterosuperior Posterosuperior Lateral Anteroinferior
Right middle	.....	Anteromedial Posterolateral
Right lower	Dorsal	
	Basal	Anteromedial Posteromedial Anterolateral Posterolateral

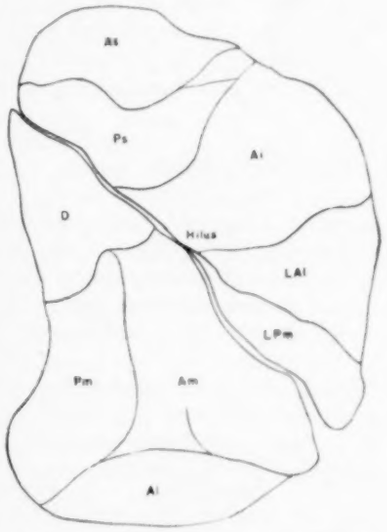


Fig. 13.—Left lung, medial view: *As*, anterosuperior segment; *Ps*, posterosuperior segment; *Ai*, anteroinferior segment; *D*, dorsal divisional segment; *LAi*, anterolateral segment of lingula; *LPm*, posteromedial segment of lingula; *Am*, anteromedial segment; *Pm*, posteromedial segment; *Al*, anterolateral segment.

Neil, J. H.; Gilmour, W., and Gwynne, F. J.: Bronchopulmonary Segments: Radiological, Pathological and Bronchoscopic Considerations, with Special Reference to Subapical Bronchopulmonary Segment, M. J. Australia **2**: 165-172 (July 31) 1937.

Behr, E., and Huizinga, E.: On the Division of the Lung Segments in the Right Upper Lobe, Acta radiol. **19**: 399, 1938.

Neil, J. Hardie; Gilmour, W.; Gwynne, F. J.; Main, Wallace, and Fairclough, W. A.: The Anatomy of the Bronchial Tree and Its Clinical Application, Australian & New Zealand J. Surg. **8**: 118 (Oct.) 1938.

Pierret, R.; Coulouma, P.; Breton, A., and Devos, L.: Étude anatomique de la zone dorsale moyenne du poumon (lobe moyen postérieur de Deve, sommet de Fowler), Ann d'anat. path. **15**: 233 (March) 1938.

Nelson.[5]

5. Nelson, H. P.: Postural Drainage of the Lungs, Brit. M. J. **2**: 251 (Aug.) 1934.

6. Churchill, E. D., and Belsey, Ronald: Segmental Pneumonectomy in Bronchiectasis: Lingula Segment of Left Upper Lobe, Ann. Surg. **109**: 481 (April) 1939.

The identification of portions of divisions brings one to the smallest unit of lung tissue of practical diagnostic or therapeutic importance at the present time, the bronchopulmonary segment. This we define as a subdivision of the pulmonary lobe delimited by avascular, diverging planes which may or may not be indicated by complete or partial fissures. Its apex lies in the hilus and its base fills an area on the lung periphery. It is supplied by integral bronchi and blood vessels, which vary in the manner of origin and intercommunication with the hilus but are fairly constant in their end distribution.

The right upper lobe is considered to consist of four segments, named anterosuperior, posterosuperior, anteroinferior and lateral. The right middle lobe consists of anteromedial and posterolateral segments. The lower lobe has two divisions, dorsal and basal. The dorsal division requires no subnames at this time. The basal division is characteristically divided into posteromedial, posterolateral, anteromedial and anterolateral segments. The left upper lobe has two divisions, one the lingular and one the apical. The lingula divides into anterolateral and posteromedial branches. The apical division separates into segments in a similar manner to the right upper lobe.

A frequent cause of confusion has been the variations of the smaller bronchi in their arrangement, both with respect to point of origin and to number visible bronchoscopically. Sometimes, for instance, only two segmental bronchi are visible at the end of a lower lobe bronchus, and occasionally all four are clearly seen, but the underlying subdivisions into bronchopulmonary segments are maintained beyond the hilar variations. Dissections and injections have shown that the segments described, surrounded by planes of avascular tissue, uncrossed by bronchi or blood vessels beyond the hilus, are found with remarkable constancy in the periphery of the lungs. In the hilus the segmental integrity is lost in a maze of interlacing bronchi, arteries and veins, varying from case to case and thus far defying exact classification.

SUMMARY

Bronchography has become an essential diagnostic aid in the investigation of many thoracic problems. An accurate, complete, intelligently made bronchogram can reasonably be expected of any one who undertakes the procedure. A simple, almost uniformly successful technic which is suitable for general use has been developed.

An adequate, accepted bronchial nomenclature is lacking but hoped for by a majority of workers in the thoracic field. A terminology is proposed to meet the practical needs of internists, radiologists, bronchologists and surgeons. Simplification and reduction of confusion are hereby sought.

ABSTRACT OF DISCUSSION

DR. CHEVALIER L. JACKSON, Philadelphia: The importance of bronchography is universally recognized now, and most thoracic clinics require the mapping of all five lobes of the two lungs before an operation such as lobectomy or pneumonectomy is attempted, certainly before it is done for bronchiectasis. I agree with the great efficacy of the technic which Drs. Adams and Davenport have described. This technic is very similar to one that we decided was most convenient for our needs. Dr. Maurice Bonnier and I described that technic about four years ago before the American Bronchoscopic Society, and the description was published in the *Annals of Otology, Rhinology and Laryngology* for September 1937. We had a number of years before that given up the use of the bronchoscopic method of instillation of iodized oil because the catheter method has many advantages. We do not find it necessary to use a swab application in anesthesia. We use a spray and instillation of anesthetic solution preliminary to the introduction of the catheter. The posturing of the patient has been beautifully illustrated by the authors. As was shown, however, it is necessary to change the posture according to the portion of the bronchial tree which we wish to fill. I think they are very ambitious to attempt to fill all lobes of both lungs at one sitting, but under the most favorable conditions that can be done. It is our practice to do the study in two sittings, mapping the more involved one first, and then at a second sitting a few days later, or a week later, mapping the other lung. It is very important to insist on the use of oblique films if the two lungs are filled at the same sitting. I am in full agreement with the relative contraindications that have been mentioned. These contraindications are relative and not absolute. In 1939 I had the pleasure of seeing Dr. Hardie-Neil demonstrate the "bronchopulmonary segments" with the inflation method, using the prepared specimen and inflating each segment separately with a little air bulb and glass catheter. Ever since I saw this demonstration, in Honolulu, I have been working along with Dr. Huber of our department of anatomy on this subject. The importance of the segmental bronchus and the bronchopulmonary segment is definitely established. The bronchoscopist and bronchologist deserve the credit of pointing out the importance of the anatomy of the bronchi and lobes in thoracic disease. A number of years ago the bronchoscopists and bronchologists began insisting on lateral films, even before the bronchographic studies became routine in the study of these cases. Now, with the recognition of the conception of the segmental bronchi and the bronchopulmonary segment a further practical advance has been made.

DR. LOUIS H. CLERF, Philadelphia: I am interested in the presentation of Drs. Adams and Davenport, particularly in the multiposturing of the patient during mapping of the individual lung. This is one of the great difficulties, namely, to get the iodized oil in the desired location; obviously the catheter method has simplified this. It is not readily accomplished by the bronchoscopic method. For that reason I have been employing the catheter method for some time, using the coudé catheter and in certain instances the Thompson catheter. I wish to ask what type of catheter the authors employ. The nomenclature that is suggested seems practical. After all it must be based on anatomic distribution of the bronchi. It is necessary that we all use a common language in describing the tracheobronchial tree so that internists, surgeons and roentgenologists will be able to interpret our findings.

DR. RALPH ADAMS, Boston: I am grateful to Dr. Jackson for giving credit to previous workers who have studied this problem, and much of their work has been of a very high order. Ewart in 1889 was the first to direct attention to this subject and wrote a classic monograph on it, which can now be obtained only with difficulty. Neil, Jackson, his co-workers, Baker and many others have contributed. The technic of anesthesia was not elaborated, as we believed it to be superfluous before this group. A number 16 ordinary urethral catheter is commonly employed by us. In a previous publication we discussed the merits of the Thompson catheter for serial selective bronchography, as may be employed for the limited or localized study of special segments in particular cases. The oil should be injected at room temperature rather than warmed, because this minimizes alveolar filling, which in turn allows better study of the bronchial pattern and reduces complications which might arise, such as pneumonitis. The nomenclature proposed has been submitted informally to a number of leading thoracic clinics through their chiefs of service, Drs. Graham, Alexander, Eloesser and Doley, and I hope that Dr. Clerf has considered it also to determine whether they would be willing to accept this proposal or to accept it with modifications which they might suggest. We hope that this proposal, or a modified one, may become commonly used.

INTRAVENOUS ANESTHESIA

PAUL W. SEARLES, M.D.

BUFFALO

The simplicity of administration and the lack of detrimental effects of the short acting barbiturates have tended to increase their value for intravenous anesthesia greatly.

The historical background for intravenous anesthesia began with the use of chloral hydrate in 1872 by Ore of France. Following this, a group in Petrograd first used hedonal (methyl propyl carbinol urethane) in 1905. The volatile anesthetics were then used. Ether was given in saline solution intravenously by Burkhardt of Germany in 1909, and chloroform also had a brief trial. In this country Noel and Scuttar first used paraldehyde for this purpose. A brief trial was given ethyl alcohol by Marin of Mexico City in 1929. Avertin with amylene hydrate, first used in 1929 by Kirschner in Germany, had but little intravenous use. None of these received general recognition for intravenous anesthesia.

The first barbiturate to be administered intravenously was somnifen, a mixture of barbital and dial, and was introduced in 1924 in France by Fredet and Perlis. This preparation was subsequently changed to barbital and alurate. Pernoston was introduced by Bumm in Germany in 1927 and is still being occasionally used. It was probably the best intravenous anesthetic to be used prior to evipal. Following this, sodium amytal was introduced in this country in 1929 by Zerfas. Pentobarbital sodium (nembutal) was tried in 1930 and found to produce a prolonged postoperative sleep.[1] Evipal soluble was first used in Germany by Weese and Scharpff in 1932. Pentothal sodium was introduced by Lundy and Tovell [2] in 1934. There have been a few barbiturates, namely, soneryl, eunarcon, methyl luminal and thio amytal, which have been introduced in the recent years but which do not appear to have particular merit as intravenous anesthetics.

Thus far the short acting barbiturates evipal soluble and pentothal sodium have proved the most satisfactory agents for producing intravenous anesthesia. Pentothal sodium is more potent than evipal soluble and affords greater surgical relaxation.

During the last six years I have had the opportunity of personally administering over two thousand anesthetics with short acting barbiturates and to observe the use of these drugs by other anesthetists in a like number of cases.

INDICATIONS

It is my purpose to suggest that intravenous anesthesia with pentothal sodium and evipal soluble can be used in certain major as well as minor operations and to emphasize their advantage for the "poor risk patient."

Where the short acting barbiturates are used in certain types of major operations they should be given in conjunction with other methods of anesthesia such as avertin with amylene hydrate, local block or nitrous oxide-oxygen. Brain surgery at the Buffalo General Hospital has been performed for the last two years under a combination of anesthesia which consists of a basal dose of avertin with amylene hydrate, an infiltration of the line of incision with 1:15,000 nupercaine solution and intermittent doses of sodium pentothal. Rarely is there more than 1 Gm. of pentothal solution required for the entire procedure, which may take from four to five hours. A three way stopcock is fitted to a continuous intravenous drip and serves to administer both the anesthetic and fluids as desired. If the airway is inadequate an intratracheal tube can be inserted. Oxygen can and should be administered. This combination of anesthetics is ideal for brain surgery and I think greatly reduces the element of shock.

The administration of pentothal sodium to supplement an abdominal wall block and splanchnic block in a gastric resection results in good surgical relaxation with a minimum of shock for the patient. The intravenous anesthetic is administered in conjunction with a continuous intravenous drip as described. The intravenous anesthesia relieves the pain that may be caused subsequent to locating and injecting the splanchnics and also makes it possible to close the abdomen without straining on the part of the patient. If the patient is allowed to regain consciousness during the major part of the operation, it is seldom that more than 1 Gm. of pentothal solution is required for the operation. Oxygen should be administered continuously during the operation.

Previous experiments [3] on dogs led me to believe that the barbiturates possessed a tendency to protect the animal organism against shock. Seely, Essex and Mann [4] found that the onset of shock was delayed in animals given sodium amytal anesthesia as compared with those given ether anesthesia. Subsequent clinical experience has substantiated this contention and we are now using pentothal sodium in order to prevent shock in the "poor risk patient." Individuals with severe anemia, debility or senility tolerate pentothal very well. Lundy and his co-workers [5] state that "the site of destruction of this thiobarbiturate is not known definitely at this time. The drug leaves the blood stream within a few minutes of its introduction and its effects on most patients who have disease of the liver and kidneys does not appear to differ greatly from its effect on patients with normal organs. Therefore we do not feel that intravenous anesthesia is contraindicated when disease of the liver or kidneys is present but it is wise to exercise greater caution with its administration." We have found that the diabetic patient tolerates the short acting barbiturates very well and feel that some of the decrease in our mortality in diabetic amputations can be attributed to their use. Fractures in the old age group, especially those of the hips, are well handled under intravenous anesthesia. It is well to avoid the use of morphine in this old age group, as the incidence of pulmonary complications may be increased when it is used. It is also important that a light anesthetic should be used throughout the entire anesthetic period.

The greatest use of intravenous anesthesia is found in minor surgery in which profound muscular relaxation is not required. Thus in a great variety of procedures such as breast biopsies, rib resections, dilation and curettage, vaginal perineal repair, removal of painful dressings, reduction of fractures, skin grafts, cytoscopy, certain cases of prostatic resection and numerous opera-

From the Buffalo General Hospital.

Read before the Section on Anesthesiology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Lundy, J. S.: Experience with Sodium Ethyl (1 Methyl Butyl) Barbiturate (Nembutal) in More Than Twenty-Three Thousand Cases, S. Clin. North America **11**: 909-915 (Aug.) 1931.

2. Lundy, J. S., and Tovell, R. M.: Annual Report for 1934 of the Section on Anesthesia, Proc. Staff. Meet., Mayo Clin. **10**: 257-272 (April 24) 1935.

3. Searles, P. W.: The Effect of Certain Anesthetics on the Blood, J. A. M. A. **113**: 906-909 (Sept. 2) 1939.

4. Seely, S. F.; Essex, H. E., and Mann, F. C.: Comparative Studies in Traumatic Shock Under Ether and Sodium Amytal Anesthesia: Experimental Research, Ann. Surg. **10**: 332-338 (Sept.) 1936.

5. Lundy, J. S.; Tuohy, E. B.; Adams, R. C., and Mousel, L. H.: Clinical Use of Local and Intravenous Anesthetic Agents: General Anesthesia from the Standpoint of Hepatic Function, Proc. Staff Meet., Mayo Clin. **16**: 78-80 (Jan. 29) 1941.

tions of this character, intravenous anesthesia is satisfactory. Esophagoscopy and bronchoscopy can be satisfactorily performed under anesthesia with pentothal sodium, provided a fairly deep anesthesia is obtained before the insertion of the instrument. Preliminary cocainization of the throat should be carried out.

Certain uses have served to broaden the field of intravenous anesthesia. An intravenous anesthetic is valuable as a preliminary to the induction of an inhalation anesthesia to eliminate the fear which some patients have of a face mask. Likewise the pain experienced by some patients in the performance of certain local or regional blocks can be eliminated by preliminary administration of pentothal sodium. This method also can be used successfully to prolong spinal anesthesia or to prevent the accompanying nausea. However, the intravenous administration of the barbiturate during spinal anesthesia should be done cautiously in order to avoid a decided drop in blood pressure or slowing of respiration. Intravenous anesthesia as a preliminary induction to nitrous oxide-oxygen anesthesia for dental extraction has proved satisfactory in our hands. The use of intravenous anesthesia as a means for eliminating the explosion hazard in the operating room is especially valuable when a cautery or an electrical appliance is to be used.

ADMINISTRATION

A preliminary medication of pentobarbital sodium, morphine and atropine can be given to advantage before the intravenous use of pentothal sodium. The morphine and pentobarbital sodium greatly decrease the amount of drug necessary to use, and the atropine minimizes the possibility of laryngeal spasm, coughing and hiccups.

The administration of pentothal sodium is accomplished by the intermittent injection of a 2.5 per cent solution of the drug. My technic consists in a preliminary test dose of 1 to 2 cc. of the pentothal sodium solution to determine the relative tolerance which the patient has for the drug and also to prevent any danger of giving too large a dose on induction. This inductional tolerance varies greatly with each patient. I have found that as little as 2 cc. of a 2.5 per cent solution produced sufficient anesthesia in a debilitated patient to perform a complete amputation of an arm, while in other cases 1 Gm. of pentothal sodium failed to render the patient unconscious. After the preliminary injection has been accomplished the patient is asked to count, and while he is counting 1 to 2 cc. of the solution is injected at intervals until the patient is unconscious. The presence of surgical anesthesia is elicited by the lack of response to painful stimuli. Further small doses are injected when the anesthesia becomes too light.

Overdosage results in imperceptible respirations and later cessation of respirations accompanied by the development of cyanosis. Treatment consists in stopping the administration of the intravenous anesthetic, establishing an airway and performing artificial respiration. Oxygen and carbon dioxide should be administered and respiratory stimulants such as nikethamide, metrazol or picrotoxin should be injected intravenously in sufficient dosage to obtain a stimulation of respiration.

CONTRAINDICATIONS

The administration of large doses of these short acting barbiturates should be avoided because of the possible sequelae, such as a long postoperative depression or in some cases the occurrence of toxic symptoms manifested by an elevation of temperature or a rash. The dose can always be decreased when necessary by supplementing the intravenous anesthetic with other types of anesthesia. It is well to avoid the use of intravenous anesthesia in patients with a cardiac history. This is especially true in patients suffering from dyspnea, whether it is of cardiac or of pulmonary origin. Pentothal is not always a good anesthetic for children under 10 years of age because of their small veins and because of the greater need for oxygen. However, if oxygen is administered to the child in conjunction with the intravenous anesthesia and great care is taken not to produce a profound anesthesia, pentothal sodium will prove satisfactory. Operations about the nose and throat should not be done under intravenous anesthesia unless blood or mucus can be cleared from the passageways and an efficient airway maintained at all times. The use of pentothal sodium in a patient who is receiving a drug containing sulfur is debatable, as there may be a cumulative effect. Evipal soluble can be used without fear of administering too much sulfur.

SUMMARY

The use of short acting barbiturates is not confined to minor operations. Small doses of pentothal sodium given intravenously will produce satisfactory anesthesia for major operations, provided other methods of anesthesia such as avertin with amylene hydrate, local block or nitrous oxide-oxygen is used in combination with the intravenous anesthesia. Pentothal sodium may be used to advantage for the "poor risk patient" because of the protective action against shock which is exerted by the barbiturates. Owing to the ease of administration and the type of anesthesia produced, the short acting barbiturates have become the anesthetics of choice in numerous other surgical procedures.

ABSTRACT OF DISCUSSION

Dr. Rolland J. Whitacre, East Cleveland, Ohio: The widespread use of intravenous anesthesia with the short acting barbiturates has made it necessary to advance certain definite recommendations for their use. Dr. Searles has performed a valuable service in clearly setting forth the scope of usefulness of intravenous anesthesia as well as its contraindications. I should like to emphasize the importance of the conservative use of these short acting barbiturates. By conservative I refer not to the number or variety of cases but specifically to the amount of drug used in each case. Without a doubt large doses of these drugs increase the incidence of untoward complications. Likewise technical skill, although undeniably important, is not sufficient reason for advocating the routine use of unsupplemented intravenous anesthesia with the short acting barbiturates. Dr. Searles has indicated numerous instances in which intravenous anesthesia may be used to advantage in conjunction with other agents. Undoubtedly, this method of using minimal doses of pentothal sodium or evipal will be found to be valuable in still other surgical procedures. During the past few years my associates and I have used pentothal and nitrous oxide successfully in many of our cases undergoing thyroid surgery. With premedication, usually not more than 0.5 Gm. of pentothal is required for the entire procedure. It has been demonstrated that the use of dilute solutions of pentothal sodium materially increases the margin of safety of this method of anesthesia. It has been our experience that a 2.5 per cent solution and, on occasion, a weaker dilution of pentothal sodium is adequate to produce satisfactory anesthesia. A suitable method of supplying oxygen to the patient should always be available whenever intravenous anesthesia is administered. The advantage of pentothal sodium for major operations and poor risk cases is more apparent when minimal doses are used and, as Dr. Searles has pointed out, this is often accomplished by using pentothal sodium in conjunction with other agents.

Dr. George J. Thomas, Pittsburgh: With regard to the use of intravenous narcosis in combination with a continuous intravenous drip of solutions, patients receiving physiologic solution of sodium chloride or dextrose in combination with

pentothal sodium make a better recovery and show less toxicity to the anesthetic agent. The anesthetic and the supplemental fluid can be given through the same needle by the use of a manifold. The use of oxygen continuously is important and should not be overlooked. Dr. Searles stated that the diabetic, the anemic and old persons tolerate pentothal sodium surprisingly well. I too have found this to be a fact, provided the anesthetic agent is supported with an analeptic stimulant. It was mentioned that esophagoscopies and bronchoscopies can be satisfactorily performed under pentothal sodium, provided the throat is well cocainized and deep anesthesia is obtained before intubation is attempted. I find that the provisions he mentioned are very important for a satisfactory anesthetic when nasotracheal or orotracheal tubes are used. Dr. Searles mentioned the contraindication in heart disease. My associates and I made an extensive electrocardiographic study of patients under pentothal sodium anesthesia and failed to observe much of any deleterious effect on the myocardium or the conductive system of the heart. Therefore I believe that in only the severe type of myocarditis should pentothal sodium be considered contraindicated. We have found pentothal sodium exceptionally useful in eye surgery. I attribute our success in the use of pentothal sodium in this type of surgery to our preanesthetic preparation of the patient. The occasional sneezing that we previously experienced in eye surgery has been absent. The instillation of cocaine in the eye preoperatively cocainizes, via the nasolacrimal duct, the delicate and sensitive nerve endings of the nasal mucosa.

DR. JAMES YANICK, Hornell, N. Y.: It has been my experience with intravenous pentothal sodium anesthesia that minor operations, such as lacerations and cuts, require far more anesthesia than is required to relax the abdomen. It has been shown by workers at Cornell University Medical College that moderate amounts of barbiturates increase the sensitivity of the skin to pain, and pentothal sodium is a barbiturate. My observations with pentothal sodium anesthesia confirm their findings. We have a couple of good rapid surgeons by whom all uncomplicated appendixes are removed routinely under pentothal sodium. I have found that unless a saline drip is used the needle will clot up with blood, because so little pentothal sodium is used. After one has given enough pentothal sodium to desensitize the skin so that the incision can be made without the patient moving, one doesn't have to give another drop and one will have relaxation of the abdomen. Of course, if it is decided to do an exploratory or a prolonged operation, one can always shift to another type of anesthetic. Actually, appendectomies or abdominal operations of less than an hour, lower abdominal operations, require far less pentothal sodium than is required in repairing a 4 or 5 inch laceration from a cut from glass or an automobile accident. The first time one gives pentothal sodium, when a regional block is used, watch the reflexes of the patient very closely. So little is used that one cannot believe that the patient is anesthetized. I know that the first time I gave it for a herniorrhaphy with regional block anesthesia, when the patient was rather restless and uncooperative although the regional block was excellent, the small amount of pentothal sodium consumed where the skin was already desensitized was really marvelous.

DR. HAROLD D. GREEN, Cleveland: I should like to ask the author if he has had any experience with chloralose A. We have been using it in the Department of Physiology at Western Reserve for two or three years and have found that in animals it is a very satisfactory anesthetic. It acts fairly rapidly yet not quite so rapidly as evipal. The animals have apparently a higher blood pressure and withstand operation better, and it is our impression that we can withdraw more blood from an animal before his blood pressure drops to shock level than we can with some of the other barbital anesthetics.

DR. F. M. SUMMERVILLE, Oil City, Pa.: One doesn't find any deaths recorded, or practically none, but if one meets the fellows in the hall they can tell of a number of deaths. Ten different ones have told me about such deaths since I have been here. I should like to hear something about the deaths from intravenous anesthesia.

DR. PAUL W. SEARLES, Buffalo: I am very grateful to the discussers for bringing out certain points that I was unable to cover because of the time allotted and for enlarging on certain points, especially the contraindications, and the use of continuous oxygen throughout long operations. Dr. Whitacre emphasized the importance of the administration of small doses of pentothal sodium. Only by giving many of these intravenous anesthetics can one determine how small a dose will prove to be satisfactory. Of course, after the surgeon becomes accustomed to the use of intravenous anesthesia, a little movement now and then on the part of the patient is not too objectionable. It is important with administration of intravenous anesthesia in long operations that a patent needle should be maintained. Dr. Thomas emphasized the administering of pentothal sodium in conjunction with saline solution. I think that the manifold apparatus which he uses is very satisfactory. Intravenous anesthesia has been found to be a safe anesthetic when properly administered by a trained anesthetist. In answering the question tendered by Dr. Green, I do not believe that chloralose A has been used on human subjects. As to the deaths from pentothal sodium, I want to say that I have never had a patient die from the administration of pentothal sodium. I find that, when an overdose has been administered, the effects can be counteracted by giving artificial respiration and oxygen. If contraindications are carefully watched, the percentage of deaths will compare favorably with other types of anesthesia.

SPONTANEOUS CONVULSIONS FOLLOWING METRAZOL TREATMENT

ERICH LIEBERT, M.D.
ELGIN, ILL.

Opinion regarding the occurrence of epileptic convulsions in cases of uncomplicated schizophrenic psychosis is divided. While Kraepelin, Bleuler and Marchand reported that convulsive seizures not infrequently may be observed during the course of a schizophrenic psychosis, especially in catatonic patients, other authors have expressed the opinion that epileptic convulsions are extremely rare. The latter view has been expressed especially by Vorkastner [1] and by Strauss and Steiner,[2] who critically reviewed the literature on the subject. According to them the number of confirmed reports on epileptic convulsions in cases of dementia precox is extremely small, especially if strict criteria are applied in the evaluation of the various forms of attacks which may accompany a catatonic psychosis. If one demands the presence of pupillary disturbances, clonic-tonic movements and pathologic reflexes to indicate the epileptiform character of a seizure, the number of cases of dementia precox with attacks becomes extremely small.

Strauss and Steiner found in a group of 6,000 patients whose condition was diagnosed dementia precox only 20 in whom seizures had been reported. However, the evaluation showed that of these 20, in only 1 could the authors be certain of their epileptic nature. Recktenwald [3] reported 4 cases of schizophrenia complicated by convulsions. In 1 the attacks seemed to be of a hysterical character; autopsy revealed in another a meningioma and in a third cerebral arteriosclerosis.

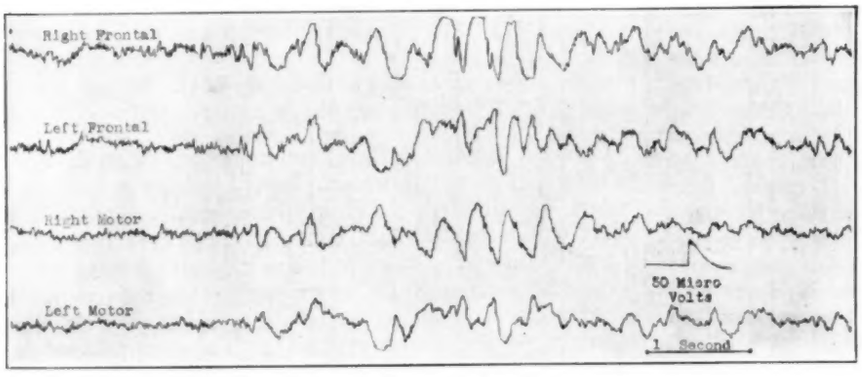
In the Elgin State Hospital, with a population of 2,564 patients with a diagnosis of dementia precox,

From the Elgin State Hospital and the Department of Nervous and Mental Diseases, Northwestern University Medical School.
Read before the Section on Nervous and Mental Diseases at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Vorkastner, W.: Epilepsie und Dementia praecox, Abhandl. a. d. Neurol. **4**: 1, 1918.
2. Strauss and Steiner, in Bumke, Oswald: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1932, vol. 9.
3. Recktenwald: Epilepsieartige Krampfanfälle im Verlaufe der Schizophrenie, Ztschr. f. d. ges. Neurol. u. Psychiat. **58**: 79, 1920.

convulsive seizures are rare. In 2 such patients autopsy revealed intracranial neoplasms, a supracellular cyst in 1 and in the other a dermoid cyst of the pineal body. In a third patient, who died during his first epileptic status after a stay in the hospital of ten years, autopsy revealed an acute swelling of the brain. The statement made by the authors that "epileptic seizures are extremely rare in cases of schizophrenia, if they occur at all." is therefore in agreement with our own observations.

However, during the last two years the number of epileptiform attacks in schizophrenic patients seems to have increased. Within a relatively short time my associates and I have seen in the hospital 7 patients in whom repeated epileptiform seizures could be observed, while concerning an eighth patient, released from the hospital, the family reported attacks of unconsciousness. It was noted that all these patients, none of whom had ever had any convulsive disorders before, had undergone a series of metrazol convulsions and that the spontaneous seizures had started some time after the cessation of metrazol therapy. Concerning none of these patients except 1 reported on by the family and not directly observed by a physician was there any doubt as to the epileptic character of the convulsion.



Slow four per second discharge of high amplitude (patient B. R.).

The seizures occurred suddenly, without any premonitory symptoms, but not before several months had elapsed after the cessation of the metrazol treatment. The sequence of events is illustrated in the following case.

B. R., a woman aged 25, was admitted to one of the state hospitals in 1938. At admission it was stated that she had always been somewhat peculiar, although she was not considered psychotic until September 1938. At that time she complained that her body was deteriorating and that she was going to fall apart. She felt that people had been talking about her. Because of the symptoms she presented, the diagnosis of dementia precox of the hebephrenic type was made and metrazol treatment advised. The patient apparently improved; she expressed a desire to return home and had some insight into the fact that she had been mentally ill. In February 1939 she was paroled after a six month stay in the hospital. Fifteen months later, in May 1940, she suffered her first spontaneous convulsion. She fell suddenly to the floor, bit her tongue and foamed at the mouth; she did not regain consciousness for about five or ten minutes. The convulsive seizures at first repeated themselves at infrequent intervals, but they became more numerous and more severe; so that it was necessary to hospitalize the patient again, this time not because of the psychosis but because of the numerous epileptic attacks. Neurologic examination showed her to have strikingly increased deep reflexes, a positive Hoffmann reflex on both sides but no evidence of any involvement of the cranial nerves. Examination of the spinal fluid revealed a cell count of 3, negative Pandy and Ross-Jones reactions, a colloidal gold curve of 1110000000, a quantitative protein estimation of 32 per cent and a negative Wassermann reaction. A roentgenogram of the skull did not reveal any evidence of increased intracranial pressure or any other pathologic condition.

During her stay in the hospital the patient had a number of convulsions characterized by sudden loss of consciousness, tonic-clonic movements and dilatation and fixation of the pupils. During these attacks she sustained several severe injuries. There was no doubt as to the epileptic character of the seizures, which were controllable only by phenobarbital. In discussing her sensations before an attack she stated that some of the seizures began with a short aura. According to her own description: "I have a sensation like I am going to have a treatment of metrazol." She described also a feeling of tenseness on the left side of her face followed by dizziness and a disagreeable sensation in the epigastrium.

Other patients on whom information has been included in the accompanying table presented the same sequence of events. Eight are listed, ranging in age from 22 to 40. All except 1 had a diagnosis of dementia precox of one of the various subtypes, and all underwent a course, some patients several courses, of metrazol treatment. None had a history of a convulsive disorder at any time, nor was there evidence of any convulsions or other epileptic phenomena prior to the use of metrazol, although some patients had been under close observation in the hospital for many years. There was no hereditary tainting. Roentgen examinations, some performed with air filling, did not reveal any evidence of a gross intracranial lesion which might be responsible for the occurrence of epileptiform seizures.

The spinal fluid examination, which included the colloidal gold test, qualitative and quantitative protein determinations, cell counts and sugar and sodium chloride determinations, gave negative results.

As can be noted from the table, the convulsions occurred at least several months after the cessation of metrazol treatment. The interval ranged from three months to two years. Further treatment had been given in only 1 case, in which convulsive shock therapy was followed by a course of induced hypoglycemic states.

The convulsions observed were uniformly of the grand mal type, characterized by sudden loss of consciousness, severe generalized tonic-clonic movements and pronounced dilatation of pupils which did not react to light. Babinski's or Gordon's reflex was temporarily present shortly after the cessation of the seizure. Neither in symptoms nor in duration did the attacks differ from the disorders seen generally in grand mal epilepsy. Only 1 patient described an aura. No definite information was obtainable from the other patients, who were too uncommunicative. The electroencephalograms of these patients showed a large variety of the changes which are usually seen in epileptic disorders and which have been described in detail by Levy, Serota and Grinker[4] as occurring in some of their cases after metrazol treatment.

4. Levy, N. A.; Serota, H. M., and Grinker, R. R.: Electroencephalographic and Clinical Studies Following Metrazol and Electrically Induced Convulsive Therapy of Affective Disorders, read before the Illinois Psychiatric Society in March 1941.

COMMENT

In 8 cases in which the diagnosis was dementia precox spontaneous convulsions occurred. The attacks started some time after the cessation of metrazol treatment. Although the 8 patients comprise only a small percentage of the schizophrenic population and of the metrazol-treated patients, it is noteworthy that the attacks occurred only in patients who had been treated with metrazol. No other etiologic factor could be discovered which might have been held responsible for the convulsions.

That paroxysmal electric dysrhythmias may be observed for several months after even a few injections of metrazol was reported by Levy, Serota and Grinker. These authors found changes in the electroencephalograms of 50 per cent of treated patients and in those of the more severely affected patients with epileptoid disturbances of the brain. Electric potentials developed characterized by three per second waves, bicuspid and tricuspid waves, spike and wave formations and substantially increased amplitude. Spontaneous epileptic convulsions were not observed by Grinker and his co-workers in their metrazol series. Read [5] briefly mentioned the fact that spontaneous convulsions were observed some time after metrazol treatment; his case was included in this study. Another case was briefly described by Hartenberg.[6]

The question of the mechanism for the production of the spontaneous convulsions arises. It is a common saying that one fit always disposes toward the next one. However, the epileptiform convulsions due to an acute intoxication are usually not followed by chronic epilepsy. Up to the present only two substances, absinth and lead, have been known to cause epileptic convulsions even a long time after their use has been discontinued. Magnan,[7] who studied this effect of absinth extensively, reported several cases of chronic epilepsy traceable to the use of absinth. Since oil of wormwood when given intravenously produces convulsions similar to those obtained with metrazol, one might be inclined to suspect a similar action for the two substances. Discussing the action of lead and absinth, Muskens [8] surmised that "in such cases the threshold is lowered or the resistance of the patient has been so completely broken down that the ordinary sequence of daily life is sufficient to provide the stimulus for the succeeding fits."

In the evaluation of our material, two facts seem to be outstanding. First, it took a considerable period—at least three months but mostly more than twelve months—before a spontaneous convulsion could be observed. Regarding this observation, one might think of the reports by Weil and his co-workers,[9] who showed that in patients who had died several months after the cessation of metrazol treatment an extensive proliferation of the glia was present, involving astrocytes and microglia. These changes were similar to those found in experimental animals by the same authors. Although there was no direct relationship between the time elapsed after the cessation of treatment and the severity of the gliosis, there were well defined individual differences in the responses to the treatment. One might be inclined to link these facts together and to surmise that in cases in which spontaneous epileptic seizures develop the scar formation in the brain tissue is responsible for the lowering of the convulsive threshold. Neuronic alterations were observed also in his patients by Weil and have been observed by many other authors in patients who had died after metrazol convulsions. Grinker, in discussing a case of spontaneous convulsions after electric shock treatment, expressed the opinion that the neurons had been damaged to such a degree that ordinary stimuli might produce a convulsive seizure. This explanation might hold true for the spontaneous convulsions following metrazol therapy. Although the neurologic examination in our cases did not reveal any definite pathologic changes, a pathologic functioning of the brain was indicated by the electroencephalogram.

The second fact which seems to be of importance is that the initial dose of metrazol necessary for the production of a convulsion was low—lower than that for the average patient receiving metrazol treatment. One might think that our patients, although they had not had any epileptic seizures before treatment, had a convulsive threshold which could easily be broken down by the administration of metrazol. This might indicate that constitutional factors play a part. Before the administration of metrazol the convulsive threshold was high enough to avert epileptic seizures, but the pathologic alterations produced by the treatment lowered this threshold to such an extent that now ordinary stimuli were sufficient for the production of a convulsion. Since autopsy reports on our patients are not yet available, a definite correlation between the pathologic changes and the clinical picture still needs to be obtained.

Data on Eight Patients with Dementia Precox Given Metrazol Therapy

Patient	Age	Sex	Diagnosis	Duration of Psychosis, Yr.	Hospitalization, Yr.	Heredity	Metrazol Treatment	Number of Convulsions	Initial Dose, Cc.	Spontaneous Seizures, Mo. After Treatment
J. K.	22	♂	Catatonic dementia precox	2	2	Normal	May 1937	25	3	3
H. K.	30	♀	Dementia precox of undetermined origin	5+	5	Alcoholism	January 1938	24	4.5	24
M. C.	22	♂	Dementia precox of undetermined origin	6	4	Normal	February 1938	16	5	23
B. R.	25	♀	Hebephrenic dementia precox	3	2	Normal	Fall, 1938	16	..	15
E. K.	22	♂	Dementia precox of undetermined origin	2	2	Normal	February 1939	15	3	9
J. J.	37	♀	Hebephrenic dementia precox	4	2	Normal	May 1939	9	3	19
H. A.	27	♂	Paranoid dementia precox	4½	4½	Normal	June 1939	53	3	18
A. C.	42	♀	Paranoid state	12	8	Normal	January 1938	..	..	17

5. Read, C. F.: Consequences of Metrazol Shock Therapy, Am. J. Psychiat. **97**: 667 (Nov.) 1940.

6. Hartenberg, P.: Epilepsie consécutive à un traitement par le cardiazol, Ann. méd.-psychol. (pt. 1) **98**: 73 (Jan.) 1940.

7. Magnan: Des principaux signes cliniques de l'absinthisme, Rev. d'hyg. **12**: 909, 1890.

8. Muskens, L. J. J.: Epilepsy, New York, William Wood & Co., 1928.

9. Weil, Arthur, and Liebert, Erich: Neuropathologic Study of Six Cases of Psychoses in Which Metrazol Was Used, Arch. Neurol. & Psychiat. **44**: 1031 (Nov.) 1940.

SUMMARY

In 8 patients epileptic convulsions developed three to twenty-four months after the cessation of metrazol treatment.

None of these patients had had any convulsive seizures prior to the metrazol treatment, although they had been observed in the hospital for many years.

As epileptic seizures in cases of dementia precox are extremely rare, the production of the spontaneous seizures was thought to be due to the metrazol therapy, metrazol being able to cause spontaneous convulsive seizures, possibly in the same manner as do absinth and lead.

In using metrazol in the treatment of functional psychoses, therefore, one should take into account the possibility of the production of spontaneous epileptic seizures even a long time after the cessation of treatment.

750 South State Street.

ABSTRACT OF DISCUSSION

DR. ROY R. GRINKER, Chicago: We should be grateful to the author for bringing the matter of late appearing defects following shock treatment to our attention. The evidence that has been gathered from electroencephalographic studies following shock treatment, whether by metrazol or electrically induced shock, is that the brain waves are pathologic for some time after treatment, showing a rhythm of three, four and six per second with large cusps of great amplitude and sometimes spike formations. It has been anticipated, as has been reported here, that many psychotic patients would eventually become epileptic through the use of shock therapy. It might be said that these individuals had the potentialities of developing epilepsy before treatment. It is unfortunate that brain waves were not taken before treatment so that they could be compared with those afterward. In my patients the curves were all normal before treatment. The statement might be made that in the schizophrenic psychoses the number of shocks given was usually far greater than in the depressions, and hence the excessive quantity may be responsible for the development of epileptic attacks. In my work I have found no correlation between the number of shocks and the characteristic abnormalities in the brain waves seen afterward. It is true that these waves gradually subside and the normal curve eventually returns. This problem brings us back again to the discussion of choice between rational therapy and the danger of long standing psychosis as against rapid relief of depression and anxiety with the signals attendant on varying damage to the brain. Does one wish to take a chance on producing rather severe brain damage or to wait in certain cases until the psychosis recedes and the patient becomes amenable to more rational psychotherapy? I cannot pass this opportunity to say that we are becoming less psychiatrists and more and more physical therapists. At one time I indicated that, with metrazol, psychiatrists hardly waited for the patient to take his clothes off before he was shocked, and now we learn from Dr. Myerson that it is not necessary to hospitalize a patient, that one can shock him in one's office, keep him there for an hour or two and then return him home. This I consider extremely dangerous, since before long such easily applied therapy will be appropriated by the inexpert and used promiscuously and indiscriminately. It is obvious that this method is less dangerous than lobotomy because recovery of memory does occur and electroencephalographic findings tend to return to normal. When one cuts the fiber pathways everything is gone and no regeneration of the central tissue is possible. After shock there is a possibility that the irritative effect of some of the acute lesions may disappear.

DR. ERICH LIEBERT, Elgin, Ill.: I only want to mention that in the last two months I have had 2 more cases in which spontaneous convulsions were observed after metrazol treatments had been given.

POIKILODERMA-LIKE CHANGES IN THE SKIN FOLLOWING ARSPHENAMINE DERMATITIS

REPORT OF TWO CASES

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AND
JEROME K. FISHER, M.D.
NEW YORK

For the past two years we have had under observation 2 patients with postarsphenamine dermatitis terminating in erythema, pigmentation, telangiectasia, atrophy and alopecia, a combination of symptoms which strikingly resembles those first described by Jacobi [1] at the German Dermatologic Congress in Berne in 1906 and named by him poikiloderma atrophicans vasculare. The body of literature on this subject is comparatively small, considering the fact that the disease has been known to the medical profession for thirty-five years. Since Jacobi's case approximately 160 others have been reported, most of them for confirmation of diagnosis before various local dermatologic societies. It is interesting to note that in only 4 of these cases was the poikiloderma or the poikiloderma-like changes in the skin regarded by the author as the sequels of a postarsphenamine dermatitis; these 4 all appeared in the foreign literature.

REVIEW OF THE LITERATURE

K. Pinter [2] reported the first case of this type before the Hungarian Dermatologic Society on Nov. 9, 1928. The patient, a woman aged 23, had received three series of neoarsphenamine injections, after each of which she had an attack of arsphenamine dermatitis. The first attack, which came on after she had received 4 Gm. of neoarsphenamine in 1926, subsided in about three months, leaving a brown pigmentation followed by telangiectasia, punctate hemorrhages, thinness of the skin and other appearances of poikiloderma.

Gruetz [3] on Oct. 12, 1930 presented before the Society of Rhenish-Westphalian Dermatologists a woman of 40 whose skin showed poikiloderma-like changes which had followed a generalized arsphenamine dermatitis. There were numerous irregular pigmentations. The body and scalp hair had almost entirely disappeared. Histologic sections showed that there were pigment deposits in the papillary bodies and that the elastic fibers had changed into small, well defined bandlike zones parallel to the epidermis.

Grau Barberá [4] cited the case of a man of 26 who was given eight injections of neoarsphenamine (totaling 4 Gm.) in treatment of a primary lesion. After the next to the last injection an itching, nonexudative, erythematous eruption was noted in the heavy folds of the skin of the elbows, axillas and knees. There was some desquamation. The patient was given two injections of a bismuth compound, after which the erythematosquamous eruption became generalized and

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Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

1. Jacobi, R.: Fall zur Diagnose (Poikiloderma vasculare atrophicans), Verhandl. d. deutsch. dermat. Gesellsch., IX. Kongress **9**: 321, 1907.
2. Pinter, K.: Poikiloderma atrophicans vasculare und Salvarsandermatitis, Zentralbl. f. Haut.- u. Geschlechtskr. **29**: 495, 1929.
3. Gruetz, O.: Poikilodermieartige Folgezustand nach universeller Salvarsandermatitis, Zentralbl. f. Haut- u. Geschlechtskr. **36**: 722, 1931.
4. Grau Barberá, M.: Contribución al estudio de los poiquilodermias: un caso de poiquilodermia secundaria, Ars med., Barcelona **9**: 329, 1933.

persisted for five months, with itching and abundant desquamation accompanied by slight loss of hairs from the eyebrows. After the erythroderma had disappeared areas of reticular atrophy were seen, distributed over the whole body but most profusely over the skin of the abdomen, flanks, thighs and Scarpa's triangle. In the atrophic areas were islands of normal skin which were slightly hyperkeratotic and showed some purulent desquamation. The hyperkeratotic areas were more pigmented than the normal skin. The skin as a whole showed a slight wrinkling comparable to that found in patients with mild xeroderma. Finely branched telangiectases were found distributed regularly throughout. The anterior region showed pigmentation, with light reticulated hyperkeratosis. There was faint pigmentation in the inguinal folds and in places where the lesions were most abundant. The mucous membranes were also involved. Both clinically and histologically the patient presented the appearance of having poikiloderma.

Covisa and Bejarano [5] reported the case of a woman aged 39 with a strongly positive Wassermann reaction who was given a total of 5 Gm. of neoarsphenamine and 2 Gm. of a bismuth compound. Before she received the next to the last injection of neoarsphenamine an erythematosquamous eruption appeared, beginning in the flexure of the elbow and finally becoming generalized and exceedingly pruritic and exudative in type. The dermatitis gradually cleared, leaving a diffuse reticular eruption with alternate zones of erythema, pigmentation and atrophy, telangiectasia and in some places a furfuraceous desquamation.

Both the clinical and the histologic changes were consistent with those of classic poikiloderma as described by Jacobi.

Epstein's [6] case, which he described as of an "unusual reticular fibroatrophoderma following arsphenamine dermatitis," might also be included here, since the changes which occurred are strongly reminiscent of poikiloderma, even though Epstein did not himself suggest any connection with that disease. After a course of neoarsphenamine injections the patient, a woman aged 41, had a typical generalized arsphenamine dermatitis which, when it subsided, left a peculiar atrophoderma over the portion of the neck which is exposed when a V-necked dress is worn. The skin over this area was thinned and inelastic. Numerous telangiectases were present. The surface was traversed by numerous keloid bands which intersected to form a network.

Histologic examination showed a thin epidermis, intracellular edema, fibrosis of the corium and some endarteritis. There were a few foci of round cells scattered throughout the cutis.

In these 4 instances of poikiloderma-like changes and the 1 of "atrophoderma" closely resembling poikiloderma the changes described occurred as a sequel to arsphenamine therapy. We found reported in the literature 4 other cases of poikiloderma-like changes, 3 of which were due to exposure of the skin to substances containing arsenic, while the fourth followed treatment with arsenic in a form other than arsphenamine.

Noguer-Moré and Grau Barberá [7] described 3 cases of follicular pigmented exogenous toxicoderma occurring in women engaged in occupations in which they came into contact with oily substances containing iron and arsenic, the parts of the skin affected being those which were directly exposed to the oily substances (hands, lower arms, face, neck and exposed parts of the chest). There was chronic or subacute inflammation around the skin follicles, with some tendency to hyperkeratoses and with hyperpigmentation or hyperemic pigmented macules in uneven distribution. The pigment was partly clumped and partly arranged in a network. No atrophy was observed.

Von Leszczynski [8] found poikiloderma-like symptoms in a man aged 35 who had received sixty-eight injections of an arsenical during the period 1916 to 1917 and more of the drug (in quantities not stated) from 1919 to 1920 for alleged pityriasis rubra; his skin showed changes typical of Jacobi's poikiloderma after exposure to wet and cold and, subsequently, to an explosion. Von Leszczynski expressed the opinion that the combination of shocks caused a later pituitary disease (insufficiency) and probably led also to the development of the cutaneous condition. He did not attempt to incriminate the arsenical in the causation of the condition, but it probably was of much more actual importance than the shocks which he stressed.

Nobl [9] in 1935 gave an excellent comprehensive discussion of poikiloderma due to arsphenamine, but he did not cite any cases.

Only a comparatively small number of papers on the subject have found their way into print. In the American literature they have been particularly few, only eight articles (by Lane,[10] Bowman and Clark,[11] Usher,[12] Taussig,[13] Oliver,[14] Keil,[15] Guy, Grauer and Jacob [16] and Hazel [17]) having appeared on the subject since Lane [17a] introduced the first American case before the New York Dermatological Society on May 25, 1920. In view, therefore, of the comparative scarcity of reported cases of poikiloderma or poikiloderma-like changes following arsphenamine dermatitis we felt that it would be of interest to present our 2 cases, in which arsenic seemed definitely to be the active agent in the production of the cutaneous changes observed.

REPORT OF CASES

CASE 1.—G. V., a Puerto Rican woman aged 32, was admitted to the Vanderbilt Clinic in April 1937 with a generalized eruption and total alopecia of two years' duration.

The patient remembered no childhood diseases. Menstruation started at the age of 12 and was always regular and normal. She was married at 18 and had one child, aged 12 years, living and well. There had been one accidental abortion. At the time of the patient's admission to the clinic her husband was being treated in a tuberculosis sanatorium. (He died in 1938.)

5. Covisa, J. S., and Bejarano, J.: Poiquilodermia vascular atrofiante consecutiva a eritrodermia salvarsánico. Actas dermosif. **25:** 233, 1933.
6. Epstein, Ervin: Unusual Reticular Fibroatrophoderma Following Arsphenamine Dermatitis, Arch. Dermat. & Syph. **37:** 987 (June) 1938.
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8. von Leszczynski, R.: Zur Pathogenese der Poikilodermie (Jacobi), Dermat. Wchnschr. **84:** 321 (March 5) 1927.
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11. Bowman, K. M., and Clark, E. C.: Case of Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **15:** 583 (May) 1927.
12. Usher, B. D.: Poikiloderma Atrophicans Vasculare: Report of Case, Arch. Dermat. & Syph. **25:** 683 (April) 1932.
13. Taussig, Lawrence: Poikiloderma Atrophicans Vasculare, Jacobi: Report of Case with Review of Recent Literature, Arch. Dermat. & Syph. **25:** 882 (May) 1932.
14. Oliver, E. A.: Mycosis Fungoides with Poikiloderma-Like Symptoms, Arch. Dermat. & Syph. **33:** 267 (Feb.) 1936.
15. Keil, Harry: Parapsoriasis en Plaques and Incipient Mycosis Fungoides, Arch. Dermat. & Syph. **38:** 545 (Oct.) 1938.
16. Guy, W. H.; Grauer, R. C., and Jacob, F. M.: Poikilodermatomyositis, Arch. Dermat. & Syph. **40:** 867 (Dec.) 1939.
17. Hazel, O. G.: Poikiloderma Atrophicans Vasculare: Report of Case, Arch. Dermat. & Syph. **40:** 776 (Nov.) 1939.
17a. Footnote 10, second reference.

Her first admission was to the obstetric department of a hospital because of pregnancy in November 1936, at which time a routine Wassermann test gave a strongly positive result (4 plus). She denied that she had had any initial or secondary syphilitic lesions. After she had received eight intravenous injections of neoarsphenamine and three intramuscular injections of a bismuth compound she had a generalized exfoliative dermatitis. In January 1936 she was referred to the gynecologic department because of a suspected abortion. Roentgenographic examination in April 1936 revealed the presence of a 6 month fetus. It could not be determined by roentgenogram whether the fetus was viable, although, because of the overlapping of the small bones and the distortion of the head, it was assumed that it was not. The patient, however, refused to allow the uterus to be evacuated.

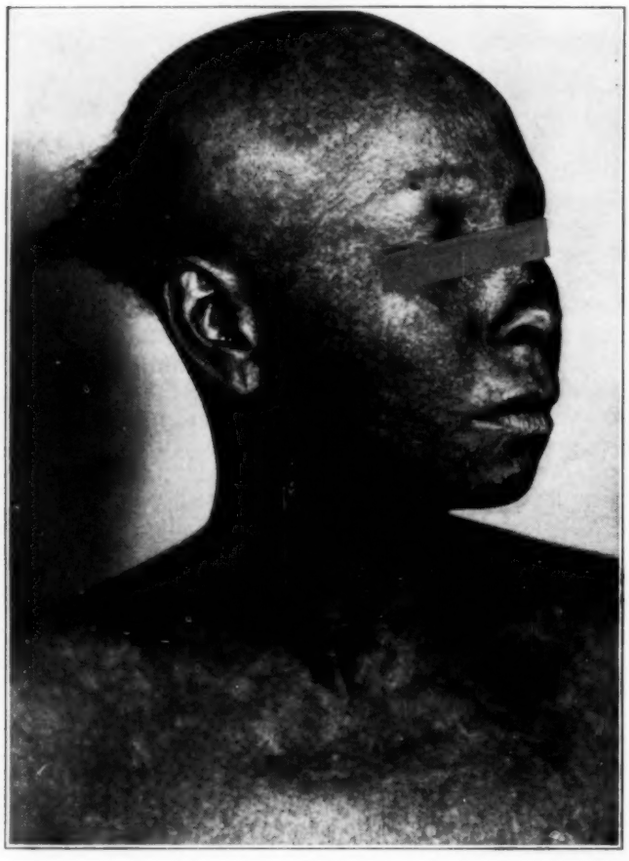

Fig. 1 (case 1).—Extensive pigmentation, areas of depigmentation, atrophy, telangiectasia, especially of the cheeks, and extensive alopecia.

At that time the skin showed little exfoliation, but there was a generalized thickening, with a papular eruption and almost total alopecia, and the skin had become much darker.

In February 1937 she visited one of the board of health clinics to continue antisyphilitic treatment, her chief complaint being impaired vision and excessive lacrimation. She was given five injections of sodium thiosulfate and was then transferred to the Vanderbilt Clinic.

Physical examination on admission to the clinic showed that she was well developed and fairly well nourished, weighing 110 pounds (499 Kg.). The general physical examination revealed no pathologic changes except enlarged and cryptic tonsils. The eyes were essentially normal, the fundi healthy and the media clear, and there was no evidence of cataract. The neurologic examination was noncontributory.

The entire skin presented a remarkable picture of extensive deep brown to black mottled, pigmented areas, together with a fine network of telangiectatic blood vessels, atrophy and total alopecia (fig. 1). The skin over the face, neck, chest and scalp was more atrophic than that of the other parts and had a decidedly reticulated appearance, with numerous small capillaries which appeared to be covered only by the thinned, atrophic, wrinkled skin. Over the skin of the abdomen near the umbilicus and on the upper posterior aspect of the right arm there were a number of pea-sized, papular, verrucous lesions. There was severe hyperkeratosis of the soles and heels and the sides of the great toes. A pea-sized cutaneous horn projected over the right eyebrow. The mucous membranes of the cheeks and the tongue showed extensive areas of leukoplakia and light brown to bluish pigmentation. The nails were not involved. Perspiration was not noticeable anywhere except on the palms and soles.

The blood count, examination of the urine, chemical examination of the blood and Aschheim-Zondek rabbit test all gave results within normal limits.

The arsenic content of the blood, determined at various intervals from 1937 to 1941, ranged from 0.005 to 0.21 mg. per hundred grams of dry blood. The skin showed 0.003 mg. of arsenic per hundred grams of dried specimen. The arsenic content of the urine measured at one time 0.03 mg. and on another occasion 0.08 mg. in a twenty-four hour specimen (670 cc.).

Spectrographic examination of the skin showed the presence of sodium, magnesium and iron, but no abnormal metallic constituents were noted.

Serologic tests of both blood and spinal fluid gave negative results.

The first intradermal test with old arsphenamine, which was made in April 1937, one year after the first appearance of the exfoliative dermatitis, produced erythema with infiltration and scaling within two weeks. After a month a nodule was formed and the erythema and scaling disappeared. The second test, made in 1940, four years after the development of the dermatitis, produced a 2 to 3 cm. area of dermatitis with a 1 cm. papule in the center.

Patch tests with old arsphenamine, made in 1938, gave negative results.

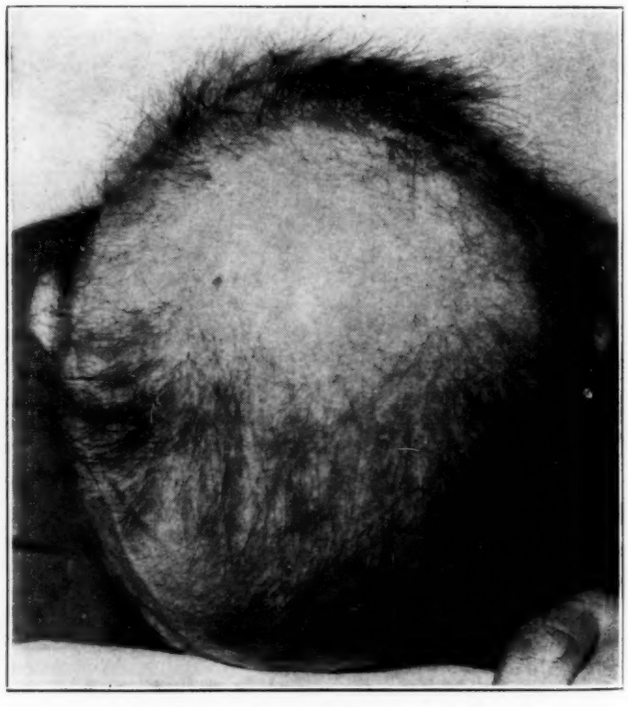

Fig. 2 (case 2).—Partial alopecia of the scalp.

Roentgenograms of the skull showed no abnormalities except calcification of the pineal body.

Histologic examination of a section from the abdomen showed severe hyperkeratosis. The epidermis showed some areas of atrophy and others of acanthosis. The corium was edematous and vascular and was the site of a chronic inflammation. Numerous chromatophores were seen. The histologic diag-

nosis was atrophy of the skin with keratosis and melanodermatitis.

Another specimen of tissue consisted of a keratotic plug resting in an epidermal invagination. Beneath this plug the epidermis had undergone acanthosis. No malignant changes were noted. There were evidences of dyskeratosis and some changes in the granular layer, such as occur frequently in patients with verruca vulgaris. In the area of greatest change the melanin pigment had disappeared. The adjacent epidermis,

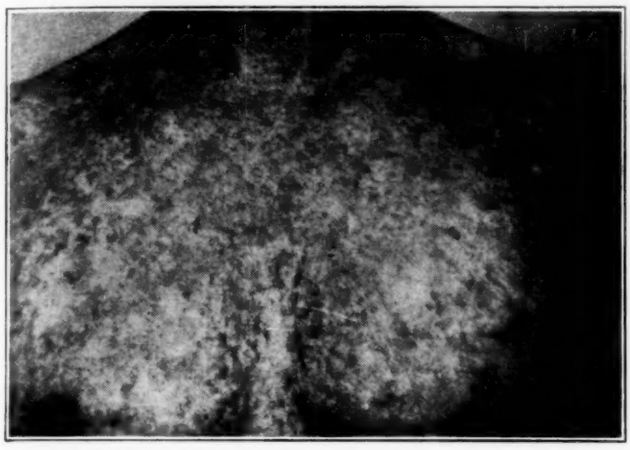

Fig. 3 (case 2).—Pigmentation, depigmentation, telangiectasia and atrophy of the chest.

however, was hyperpigmented. The corium beneath the lesion was the site of definite though not extreme chronic inflammation. The histologic diagnosis was arsenical keratosis.

From April 1937 to June 1940 the patient has received forty-two injections of sodium thiosulfate and twenty injections of bismo-cymol. She has also received liver extract, vitamin preparations and constitutional therapy as indicated.

Since she first came under observation in May 1937 her progress has been slow but gradual. The skin has become softer, and there is a sparse growth of hair in the occipital, axillary and suprapubic regions, but the other parts of the body are still entirely without hair. By June 1937 the hyperkeratotic plaques on the soles had cleared up and the skin had become lighter. In September the skin over the chest, back and arms had lost its reticulated appearance, the dark spots had entirely disappeared, the telangiectasia over the face was much less prominent than before and the scanty growth of hair on the parietal areas of the skull had improved. Black, pigmented, macular spots were still present on the thighs and buttocks. The leukoplakia of the tongue and the buccal mucous membranes had almost disappeared. By December 1937 the patient's eyesight had improved so much that she could read small print. About that time the verrucous lesions on the right arm and the left ear fell off spontaneously. In March 1938 the patient noticed that she perspired somewhat more freely than she had before. In May she underwent an operation for the removal of the fetus, which had been retained for more than two years. After operation her general health improved a great deal. In June the keratosis on the feet cleared up, but the verruca on the ear grew back. By November 1939 she had gained 10 pounds (4.5 Kg.) and felt and looked much better. The skin had become smoother and was of more normal color and texture, the atrophy was much less noticeable, and the veins on the face and chest were not so raised as before. In June 1940 new verrucous lesions appeared on the left arm, and a dark brown scaly plaque was seen on the upper portion of the left eyelid. At present the patient is feeling well. The skin on the body and the extremities is much softer and has lost practically all its spotted appearance. The growth of hair over the occipital portion of the skull is somewhat improved, although the rest of the skull is so nearly bald that the patient has to wear a wig. Her main complaint now is that because of her deficient perspiration she is unable to tolerate hot weather well.

CASE 2.—E. A., a German man aged 37, an automobile mechanic, was admitted to the Vanderbilt Clinic on Dec. 13, 1939 with a generalized eruption and alopecia of two years' duration.

The personal and family histories were noncontributory.

The patient had had none of the usual infectious diseases of childhood except a "lung catarrh." Eighteen years before, while he was in Brazil, he had had several attacks of herpes progenitalis, for which he had received only local treatment. He denied having had any sexual contacts at the time. In 1928 he had a recurrence of the herpetic lesions on the prepuce after intercourse. Two years later he received several injections of an unknown drug for "rheumatism." In December 1937 the blood showed a slightly positive Wassermann reaction, and he was given three intramuscular injections of a bismuth compound and three intravenous injections of neoarsphenamine. After the third injection of neoarsphenamine he had a severe generalized dermatitis for which he was treated with six intravenous injections of a strontium bromide preparation, without any improvement. The eruption became more severe and was accompanied by a great deal of oozing and swelling, particularly on the face, scalp and legs and around the eyes. In September 1938 the patient consulted another physician, who diagnosed his condition as a "generalized exfoliative arsphenamine dermatitis of the severest type." He was given calcium gluconate in fairly large doses and a soothing ointment (type unknown). He received also four fractional doses of roentgen rays (100 r each) on his arms, wrists and hands.

Physical examination on admission revealed that the patient was well nourished, unusually well developed and muscular and weighed about 155 pounds (70.3 Kg.). The general physical and neurologic examination gave essentially irrelevant results, except to reveal a soft systolic murmur at the apex of the heart, not transmitted.

Examination of the skin showed generalized erythroderma, with partial alopecia of the scalp, eyelids and axillary and pubic regions (fig. 2). The skin of the entire body was dry and except on the hands and feet had a bluish red tinge. Across the chest it was reticulated and mottled, in some places showing a purplish and in others a brown pigmentation (fig. 3). The skin was atrophic and wrinkled, with a fine network of

Fig. 4 (case 2).—Section stained with hematoxylin and eosin, showing atrophy of the epidermis, loss of rete pegs and variation in the melanin content of the basal layer. Note the zonal edema, increased vascularity, moderate infiltration of mononuclear cells and scattered chromatophores in the upper layers of the cutis (× 140).

telangiectatic blood vessels which gave a depressed appearance to certain areas. Numerous warty lesions were found in the axillas, on the thighs and on the lower part of the abdomen. There was severe hyperkeratosis of the palms and soles, and the buccal mucous membranes were spotted with leukoplakic areas and streaks. The scalp was atrophic and telangiectatic. Perspiration was noted on the face, hands, feet and knees only. The nails were not involved.

The blood count, chemical examination of the blood, urinalysis and Wassermann examination of the blood all gave results within normal limits.

Determinations of the arsenic content showed 0.055 mg. per hundred grams of dry blood, 0.008 mg. per hundred grams of dry skin, 0.045 mg. per hundred grams of dry stool (23.7 per cent solids) and 0.1 mg. in a twenty-four hour specimen of urine (1,470 cc.).

Coproporphyrin in a twenty-four hour specimen of urine (1,470 cc.) measured 0.01 mg.

Spectrographic examination of the skin showed no gold or bismuth present but showed silver, 0.0008 mg. per gram of dry tissue and 0.0003 mg. per gram of tissue as received.

Intradermal tests with neoarsphenamine made three years after the development of the dermatitis produced erythema and scaling within two days, a definite area of dermatitis after two weeks and in about a month a nodule which two months later had not yet become involuted.

Patch tests with various types of automobile greases and oils gave negative results.

Roentgenographic examination of the chest showed no abnormalities. Stereoroentgenograms of the skull revealed slight calcification of the frontal bone and calcification of the pineal body. The sella turcica and the rest of the skull were normal.

Histologic examination of a section from the abdomen showed that the epidermis was severely atrophic in some places. There was decided hyperkeratosis. The granular layer was extremely thin, being for the most part represented by a single line of cells. There was severe edema throughout. The melanin content of the basal cell layer varied greatly (fig. 4). The underlying corium was extremely edematous. The vascular channels were increased in number. There was a considerable increase in spindle-shaped cells. A moderate inflammatory reaction could be seen. These changes were most striking in the corium just beneath the epidermis. The deeper portions of the corium, however, were relatively free from pathologic change. Large numbers of chromatophores were found in the areas in which the melanin of the basal layers was most depleted. The elastic fibers of the superficial portions of the corium showed advanced disintegration (fig. 5). Sections stained by Fontana's method brought out strikingly the great variation in quantity of melanin in the epidermis and in the number of chromataphores within the corium (fig. 6). The histologic diagnosis was arsenical keratosis.

Histologic examination of a warty lesion from the left thigh disclosed that the skin in that region had undergone extensive

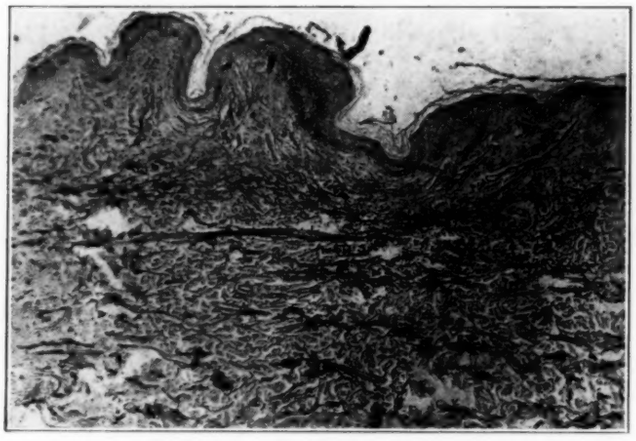

Fig. 5 (case 2).—Section stained by the Taenzer-Unna orcein method, showing disintegration and disappearance of elastic fibers in the upper layers of the cutis as a result of inflammatory changes (× 140).

hyperkeratosis and acanthosis. There was only slight parakeratosis, particularly evident over the outward projections of the epidermis. The granular layer had increased remarkably in width. Many of the granules had a coarseness such as is seen in cases of verruca vulgaris, and the individual cells were somewhat swollen. This striking change was most pronounced in places where the acanthosis had resulted in penetration of the corium by a mass of epithelial cells. The cutis was the site of a severe inflammatory reaction, with dilated blood vessels, infiltration of lymphocytes and plasma cells and proliferation of fibroblasts. Melanin, which was conspicuous in the basal layer of the uninvolved epidermis, had disappeared entirely from the verrucous epidermis. The lesion was evidently a keratosis with characteristics of verruca vulgaris.

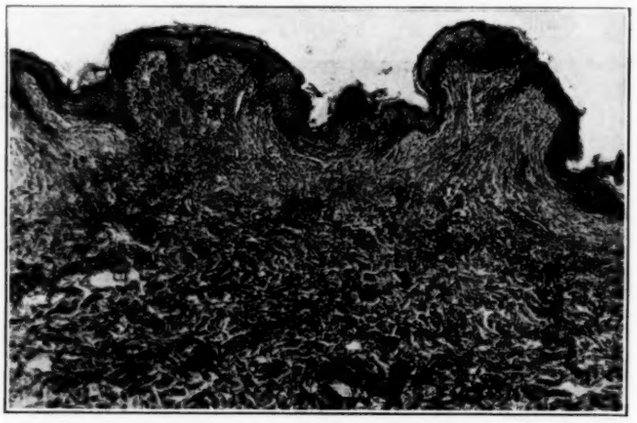

Fig. 6 (case 2).—Section stained by the Fontana method, showing variation in the quantity of melanin (× 188).

From January to November 1940 the patient received thirty-five intravenous injections of sodium thiosulfate. At present the skin is softer, and the keratotic lesions on the abdomen and the left thigh have become smaller and somewhat involuted. The alopecia, atrophy and telangiectasia are still present, but they are all much less noticeable than when the patient was first seen. There is only a slight pigmentation present in widely scattered areas. The patient's general health is good.

COMMENT

The 2 cases of poikiloderma-like changes in the skin presented here are identical as to the history and development of the dermatitis, the main difference being in its degree. In both an acute inflammatory exudative dermatitis appeared after arsphenamine treatment for syphilis. The symptoms of this dermatitis corresponded in every respect to those of an arsenical dermatitis, and the condition was so diagnosed and the patient so treated. Instead, however, of the dermatitis disappearing in the course of time, leaving no after-effects, as an arsphenamine dermatitis usually does, the skin sustained apparently permanent damage, becoming extensively pigmented and showing both light and darker colored patches of diffuse atrophy mingled with a dark red network of telangiectatic blood vessels which stood out prominently, giving the entire skin a reticulated and marmorated appearance. The skin within the network was wrinkled, thin and atrophic. There was well defined thickening of the skin of the palms and soles, especially around the heels and the great toes. On the abdomen, the upper arms and the anterior axillary folds there were pea-sized dark brown papillomatous growths.

The mucous membranes of the mouth and tongue in both cases showed widespread leukoplakic streaks or lines, a condition frequently found in greater or less degree in cases of chronic arsenic poisoning.

One of the most striking features in both patients was the alopecia, which was total in the more severely affected one (G. V.) and was accompanied by a decided atrophy of the scalp, particularly over the vertex. The alopecia in the man (E. A.) was only partial, there being a few thin clusters of hair scattered over the scalp, eyebrows and eyelashes and the axillary and suprapubic regions. Undoubtedly the alopecia can be

explained by the atrophy of the scalp. Hence it too may be regarded as more or less permanent. That it actually is may be seen from the fact that although more than four years have elapsed since alopecia developed in the first patient (G. V.), the scalp is still almost totally bald, except around the occipital region, and the vertical portion still presents a smooth, shiny, light to whitish, atrophic appearance. The body hair, too, shows only a sparse growth. The alopecia of the second patient (E. A.) is also apparently permanent, although recently he reported that hair is beginning to grow on the forearms.

Of the numerous laboratory studies made of these 2 patients only two or three need to be mentioned. The arsenic content of the blood, urine and skin was for the most part normal or high normal, only one of the several determinations made giving results at all high (0.21 mg. in the blood, in case 1). The comparatively normal figures for arsenic can probably be explained by the fact that a long interval (more than two years in each case) had elapsed between the institution of arsphenamine therapy and our arsenic determinations, so that there was ample time for most of the arsenic to be eliminated by the organism.

Roentgenograms of the skull showed slight calcification of the frontal bone in 1 patient (E. A.) and calcification of the pineal gland in both patients. We have been able to find only 1 other instance of calcification of the pineal gland in a patient with poikiloderma, namely that reported by Montgomery and O'Leary [18] before the Chicago Dermatological Society on Oct. 21, 1931. Whether or not this condition has any significance in cases of poikiloderma or poikiloderma-like changes in the skin we are not prepared to say, but in view of its rarity we feel that its presence in both our patients is interesting. The calcium-phosphorus ratio of the blood of both patients was entirely within normal limits, and no other evidences of calcification were revealed by either clinical or laboratory examination.

Treatment of both patients prior to admission to the Vanderbilt Clinic had consisted mainly in attempts to eliminate arsenic by means of calcium and sodium thiosulfate injections and the use of soothing applications. Our treatment consisted of calcium and sodium thiosulfate injections, use of a high caloric diet, administration of vitamins by mouth and for 1 patient (G. V.) removal of the petrified fetus. While the skin of both patients has shown a gradual if slow improvement, the atrophy remains, together with some telangiectasia; in both there is alopecia, almost total in the woman and partial in the man. The pigmentation has almost entirely disappeared, and the skin has practically regained its normal color. However, even though the skin may continue to improve it is probable that the atrophy and alopecia are permanent.

When we consider the clinical features of our 2 cases of postarsphenamine dermatitis—the atrophy, telangiectasia and pigmentation, the marmorated and reticulated appearance of the skin, the alopecia and the symptoms of general weakness and muscular pain—and compare them with those in the case of poikiloderma atrophicans vasculare described under that name for the first time by Jacobi [1] in 1906, we are immediately impressed by the clinical similarity of the 3 cases. Histologically, too, our 2 cases bear a close resemblance to Jacobi's, in which the main features were atrophy and hyperkeratosis of the epidermis; interstitial and parenchymatous edema and infiltration, chiefly perivascular in type; decided thinning of the granular layer; pigmentation scattered through the upper cutis, varying to a decided degree in different locations, and severe disintegration and deficiency of the elastic tissue in the superficial portions of the corium. Unlike Jacobi's case, however, in our cases there was a definite history of arsenic intake, and the dermatitis which initiated the present poikiloderma-like changes had all the characteristics of typical arsenical dermatitis. The histologic changes too suggest an arsenical keratosis.

Another feature of our cases which should be noted is that both the patients had a history of an earlier toxic condition: The first patient (G. V.) had undergone a pregnancy with subsequent retention of the fetus in the first three years of observation, while the other (E. A.) had a history of "rheumatism" which was treated by three injections of some unknown drug. The question therefore presents itself whether some other factor, perhaps a toxic one, may not have played a part along with the arsphenamine in causing the remarkable cutaneous changes or whether we are justified in assuming that these changes resulted from the arsphenamine alone. The toxic origin of poikiloderma and poikiloderma-like changes has been suggested before. It will be remembered that Ehrmann [19] in discussing Jacobi's first case suggested the possibility that the condition might be a toxic erythroderma; and there have been various other authors since who have favored the theory of a toxic origin. The question of the relative responsibility of toxic conditions and a previous arsenic intake for the development of the poikiloderma-like changes in our cases is a debatable one. Certainly although arsphenamine dermatitis itself occurs commonly, poikiloderma-like changes following it are comparatively rare, an assertion that is substantiated by the limited number of such cases reported in the literature. Hence it would seem logical to believe that it is the arsphenamine rather than the toxic factors which should be incriminated in the 2 cases reported here, though it is entirely possible that toxic conditions may also have contributed, secondarily, to the development of the poikiloderma-like changes.

Jacobi of course thought that the disease which he described was an entity distinct from any other disease described hitherto. While our cases bear a strong resemblance to the one reported by Jacobi, we feel that the changes do not represent a type sui generis but were due to an exogenous factor, namely arsphenamine. It will be remembered that Oppenheim,[20] in his masterly discussion of poikiloderma in Jadassohn's "Handbuch," remarked that this disease falls into three types: (1) the purely cutaneous type (Jacobi), (2) the congenital, neviform type (Zinsser) and (3) the type in which the poikiloderma is the end result of other, earlier cutaneous diseases, e. g. lupus erythematosus, melanoderma, lymphosarcoma, mycosis fungoides, leukemia cutis or arsphenamine dermatitis. While our cases, as we have said, show striking similarities both clinically and histologically to Jacobi's original case, etiologically they undoubtedly are of the third type mentioned by Oppenheim, since the changes seem definitely to be the end result of a postarsphenamine dermatitis.

18. Montgomery, Hamilton, and O'Leary, P. A.: Poikiloderma Atrophicans Vasculare (Jacobi)? Arch. Dermat. & Syph. **25**: 942 (May) 1932.

19. Ehrmann, in discussion on Jacobi's case: Verhandl. d. deutsch. dermat. Gesellsch., IX. Kongress **9**: 321, 1907.

20. Oppenheim, Moriz, in Jadassohn, Josef: Handb. der Haut- u. Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 635.

The question then arises: What is poikiloderma? From a review of the literature and from observation of our 2 cases of postarsenical poikiloderma-like changes it seems clear that there is in reality only one true type of poikiloderma, that originally described by Jacobi, the other types being merely variations of it, namely either the congenital, neviform type described by Zinsser or poikiloderma-like changes found in some other cutaneous disease either at the time the original disease is first observed or at some subsequent period during its course. One wonders whether if Jacobi had examined his patient for arsenic or if he had followed him over a long period he too might not have been able to classify the condition as being due to a postarsphenamine dermatitis, to a disease of the lymphoblastoma group or to some other disease in which poikiloderma-like changes occur as the result of a preceding dermatosis. On the basis of present knowledge of poikiloderma, meager though it is, one must assume that it is a symptom rather than a clinical entity, for while the term poikiloderma atrophicans vasculare is a valid descriptive one it gives no characteristic etiologic or pathologic picture to aid one in diagnosing the condition. In the last analysis we can say only that poikiloderma is a clinical descriptive term applied to a condition the main features of which are redness, telangiectasia, pigmentation and atrophy and which may be due to any one of a variety of causes.

SUMMARY

In 2 cases a postarsphenamine dermatitis ended in erythema, pigmentation, atrophy, telangiectasia and alopecia. The cutaneous symptoms presented by the patients were practically identical with those first described and named poikiloderma atrophicans vasculare by Jacobi.

CONCLUSIONS

1. Arsphenamine alone or a combination of arsphenamine and toxic factors is capable of causing poikiloderma or poikiloderma-like changes in the skin which are similar, both clinically and histologically, to Jacobi's poikiloderma atrophicans vasculare.

2. These poikiloderma-like changes result in permanent damage to the skin, the condition sometimes improving but never being completely cured.

One Hundred and Sixty-Eighth Street and Broadway.

ABSTRACT OF DISCUSSION

DR. CLYDE L. CUMMER, Cleveland: The authors' recounting of 4 cases of poikiloderma-like changes in the skin supplemented by the report of 2 observed by them establishes two points: first, that such changes may follow severe arsenical dermatitis and, second, that in seeing poikiloderma one must have in mind the possibility of an arsenical background. I have seen no such cases in the clinic where my associates and I do give a great deal of arsenical treatment, although I have to add that we have seen even less arsphenamine dermatitis or arsenical dermatitis since mapharsen has been employed. However, all have seen arsenical alopecia, I think, and a certain amount of pigmentation following exfoliative dermatitis, but not with telangiectasia. The authors' cases appear to correspond clinically and histologically to Jacobi's original report. I would like to have Dr. Cannon go into more detail, if possible, about the vitamin therapy. In the first case, as I understood, vitamins were used, but the great improvement came with the removal of the fetus. In the second case apparently vitamins had been used without any other particular factor which could be credited, and in both instances there was considerable improvement in the clinical result. I am interested in that because the statement of Dr. Cannon and his co-authors did not tell what type of vitamin therapy had been used. Dr. Duffy, of Memorial Hospital in New York, informed me that good results had been obtained by some of his confrères who had radiodermatitis of the fingers by using vitamin B, I think the complex, plus liver extract. I tried it on 1 patient with a severe radiodermatitis and was surprised to obtain distinct improvement, with lessening of the atrophy and apparently some clearing of the telangiectasia. I wonder whether or not Dr. Cannon and his co-workers could fit in the improvement with vitamins. As to their conclusions, I think we shall all be in accord.

DR. JOHN E. RAUSCHKOLB, Cleveland: According to Oppenheim's concept of the poikilodermas, they are etiologically one of three kinds: (*a*) local type as in Jacobi's original case, (*b*) congenital or nevoid type and (*c*) vasculotoxic type. In considering the vasculotoxic type under which this case report falls, three theories have evolved: First, according to Milian's view of biotropism, activating micro-organisms are present in the human host through the power possessed by potent drugs injected into the circulation, producing inflammation of these various foci of infections in the skin; second, it could be a manifestation of sensitivity or true allergy in and around the vascular loops of the skin in support of Sulzberger's theory, or, third, it can be true drug intoxication of the peripheral cutaneous circulation whose concept we know as Osborne's. In support of Osborne's work we know that the trivalent organic arsenicals locate perivascularly and produce inflammation and sclerosis of the vessels with resultant atrophy and the poikiloderma or variegated color changes along with telangiectasia so typical in postarsenical dermatitis. I am more or less in accord with the authors and with Dr. Cummer, that we have here in these 2 cases reported at least a clinical picture produced by the intravenous injection of trivalent organic arsenicals with poikiloderma-like changes. In Jacobi's original case and also in some 120 cases that have been reported since then, these atrophic cutaneous changes have been insidiously progressive with no relationship to arsenic. Perhaps the therapy that has been instituted in the authors' cases of high vitamin content diet and liver extract is the reason why they have been able to change an atrophic cutaneous pathologic condition to one of a normal picture. Probably this therapy may prove of value in the true Jacobi type of poikiloderma.

DR. MAURICE OPPENHEIM, Chicago: In my article on Atrophy of the Skin in the handbook published by Jadassohn I take the position that poikiloderma atrophicans vascularis Jacobi should not be considered any more a real clinical and histologic entity. One part of the cases of poikiloderma atrophicans vasculare Jacobi is dermatitis atrophicans progressiva. Another part, like the cases of Petges and Clezat on the neck, are partly lupus erythematosus or partly caused by local influences. The third group—and to this group belong the 2 referred cases—are secondary changes of the skin caused by other skin diseases as lichen planus or by medication. In the Viennese Dermatological Society I presented several cases, in which such local or general influences were the cause of a typical clinical and histologic picture of poikiloderma atrophicans vasculare Jacobi. Therefore I believe that we must not complicate our science by introducing new clinical pictures. If one studies the dermatitis atrophicans group, as dermatitis atrophicans cutis idiopathica progressiva, one learns that Jacobi reported in 1906 a case of the later stages of dermatitis atrophicans progressiva. In this stage one finds the telangiectasias and follicular keratosis, and histologically the degeneration of the elastic and connective tissue fibers is present as is seen in the wonderful histologic slides of Dr. Cannon and his collaborators. If one looks over one's cases of poikiloderma atrophicans vasculare Jacobi, one will observe that the poikiloderma atrophicans vasculare is not a new clinical entity as Jacobi meant.

DR. A. BENSON CANNON, New York: Dr. Oppenheim was my teacher for a brief time many years ago; I am happy to see that he has much the same idea with regard to this condition that I have tried to emphasize here. Dr. Cummer spoke of the vitamin therapy that was given to these patients. Undoubtedly it was the liver extract and the vitamin B, given both hypodermically and by mouth, that was responsible for the increased general health and well-being that resulted. Whether the improvement in the appearance of the cutaneous symptoms was due also to the medication received is rather difficult to

say. Of course, the most pronounced change took place in the woman patient, after the removal of a petrified fetus. She gained 10 pounds within a few weeks and felt and looked much better. I have an idea that if one cushions atrophic skin with an excessive amount of fat one will automatically have mechanical improvement in appearance, even though the histologic atrophy will still be present. Unfortunately the pictures shown here were not taken until about three and one-half years after the patients had their initial dermatitis. One can, I believe, say pretty definitely, though, that the skin still shows the same degree of atrophy, and the scalp the same amount of alopecia, as existed in the beginning. It is almost inconceivable that there will ever be a complete return to normality in these respects, no matter what we may do by way of treatment. We are forced to believe that, although there has been a decided improvement in the appearance and general health of both patients, the underlying histologic changes must be regarded as permanent. Five years have passed, and the woman patient still has to wear a wig and will probably always have to do so, while the atrophic areas in the skin of both patients are no less atrophic, nor are they likely to become so.

TREATMENT OF GONORRHEA AT FITZSIMONS GENERAL HOSPITAL

A STUDY OF CASES FROM SEPT. 1, 1938 TO OCT. 31, 1940

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AND
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DENVER

Our purpose in presenting this study of the results of treatment in 178 consecutive cases of gonorrhea treated during a period of twenty-six months is to report the results of newer methods of treatment and to set forth certain impressions gained from our experience on which a practicable treatment regimen can be based.

At Fitzsimons General Hospital from November 1935 to Nov. 1, 1940 the treatment of gonorrhea has been a responsibility of the Fever Therapy Department, and one of us (D. B. P.) has been in charge of this department since Sept. 1, 1938. During the period covered by this study the type of treatment has been changed from almost entirely fever therapy to almost entirely chemotherapy. Although the latter means of therapy has been carried out in another ward, all examinations of urethral and prostatic smears have been done in the Fever Therapy Department and the actual individual treatment of each patient has been dependent on the appearance of these smears.

Although all types of gonorrhea are included in this series, this report deals only with the results of treatment in the genitourinary infection.

The stain used is a modified Gram's stain, modified in that the smear is overstained with safranin, and decolorization is the final step in the process. This modification of the original Gram method of staining as used by the Fever Therapy Department, Fitzsimons General Hospital, is given in detail because adherence to this detail results in a clear, sharply stained smear, of which the bacteria show the Gram characteristic, and the cellular elements show certain typical staining characteristics to be described later.

From the Medical Service, Fitzsimons General Hospital.
All photomicrographs were made on Eastman Spectroscopic Series S Type II plates with Wratten 25 filter on light source.
Members of the Laboratory Service, Fitzsimons General Hospital, made the photomicrographs and checked the staining technic described. The careful records of cases by the Medical Officers have made this report possible.

MODIFIED GRAM'S STAIN

Reagents:

1. Crystal violet, saturated alcoholic solution, 1 part; ammonium oxalate, 1 per cent aqueous solution, 4 parts.
2. Gram's iodine-potassium iodide: iodine 1 Gm., potassium iodide 2 Gm., distilled water 300 cc.
3. Counterstain: safranin, 1 per cent aqueous solution.
4. Decolorizer: 20 per cent acetone in 95 per cent alcohol.

Technic:

1. Apply crystal violet for one and one-half minutes, wash, blot and dry.
2. Treat with Gram's iodine for one and one-half minutes, wash, blot and dry.
3. Apply counterstain for three to four minutes, wash, blot and dry.
4. Decolorize with acetone-alcohol until no further traces of violet can be detected in the decolorizer, wash and dry.

Smears stained in this manner are shifted to the blue side so that the nuclei and cytoplasm of the pus cells are differentially stained.

All the patients who were the subjects of this report had urethral or prostatic smears containing gram-negative diplococci morphologically identical with gonococci, and "cures" reported relate only to this type of infection and not, for example, to the cure of any complicating arthritic process.

Since certain cases are said to be cured, a definition of the word "cured" is necessary. To be considered cured, of course the patient must be symptom free. The other essential is that the doctor must be convinced that the patient is cured. This conviction is based on examination of the urethral or prostatic smears microscopically. After three consecutive smears which show satisfactory improvement and are negative for gonococci are obtained, a sound is passed and 0.5 per cent silver nitrate is instilled. If, after this, three consecutive satisfactory smears are obtained, the patient is regarded as cured. Whether or not a certain smear is satisfactory is the crux of the whole situation.

Examination of the smears is done by the doctor himself, and, on the appearance of the smear, further treatment, change in treatment, discontinuance of treatment, as well as delay for further smear examination is determined. Here it must be stated that this delay is very important, because, although no gonococci can be found, it is frequently obvious to the examiner that the patient still has an active gonorrheal process. As will be noted in the accompanying photomicrographs, which were taken with a Wratten 25 filter over the light source, with healing there are very definite changes in the character of the cellular elements of the smear. The changes noted in healing are quantitative, qualitative and in color. Quantitatively the pus cells grow fewer and the gonococci disappear. Qualitatively the pus cells may become fragmented (especially after fever therapy) or may become more distinctly demarcated with pyknotic nuclei, later to undergo karyolysis. The general change in color of the pus cells is from entirely red cytoplasm and nuclei in the fresh case to very dark pyknotic nuclei with pale pink or lavender cytoplasm in the healing case. The changes described are the microscopic characteristics of cell necrosis. Karyorrhexis is seen especially after fever therapy, while after successful chemotherapy the slower changes of cell necrosis as typified by pyknosis and karyolysis and a

shift toward the blue staining side are characteristic. The implication of these changes is clear. If it can be assumed that the cellular exudate is in direct response to the presence of living gonococci and then if day by day that cellular exudate shows progressive cellular necrosis with the addition of no new, fresh pus cells,

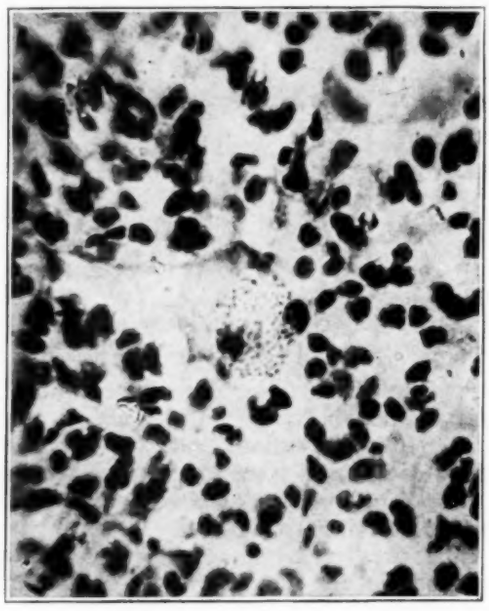

Fig. 1 (case 1).—Urethral smear positive for gonococci, Oct. 21, 1938; × 1,000.

it is evident that the exciting cause of the exudate no longer exists. The therapy itself may accelerate this cellular necrosis but will not prevent the influx of new cells except by therapeutic effect on the gonococci. On the other hand if, as may be expected from chemotherapy, these same necrotic changes are seen in a great majority of the pus cells yet there are found even a few new, fresh pus cells, it is evident that the exciting cause of the exudate is still present, though diminished. On this concept our criteria of cure and our indications for therapy rest. Our method of staining causes the characteristics of cell necrosis to become apparent, and the danger of overdecolorization is minimized. To the experienced examiner the appearance of the smear is indicative of the state of the patient's gonorrhea, and treatment is ordered accordingly. Certain patients have been kept in the hospital for many days and even weeks after the minimum number of smears have been negative for gonococci but have not been satisfactory otherwise, almost invariably to substantiate the examiner's belief that the patient was not cured. It is regrettable that the patients we regarded as cured were not checked by cultural methods. Thus it is that only 3 patients have been returned with further gonorrhea, each of these giving symptoms of acute new gonorrhea, history of exposure without prophylaxis, and symptom free periods for over six months. One of these was followed by monthly smear examination in fever therapy. Rightly or wrongly we believed these to be new infections.

Adequate treatment with the various agents to be described consists of:

(*a*) Sulfanilamide: Eight Gm. a day for three days; 4 Gm. a day for five days.

(*b*) Sulfapyridine: Thirteen Gm. the first day, then 1.5 Gm. a day for eight days.

(*c*) Fever Therapy: Nine hours of fever therapy at a rectal temperature of 106.8-107 F. given in such fashion that if more than one treatment is employed such treatments are not more than four days apart.

Such treatments with sulfanilamide and sulfapyridine as described may be considered as our routine, but in the last year, if the patient on an adequate sulfanilamide regimen did not show what was considered to be an adequate response in his smears by the fourth day, despite marked symptomatic improvement, he was immediately treated with sulfapyridine. In considering this amount of fever therapy adequate, we realize that for each case there is an amount of fever that will cure the gonorrhea, and it is only to have some point of departure that the amount stated is selected. Actually the minimum should be ten hours; if divided into treatments, they should be no further apart than on alternate days. If given further apart than this, we believe that the hours of fever cannot be regarded as cumulative therapeutically, and if given on succeeding days that the hours may be regarded as absolutely cumulative. If this belief is true, it explains why patients who have been given over fifty hours of fever therapy in weekly doses of about five or more hours remain positive for gonoccocci, whereas in these same patients two five hour treatments on successive days result in immediate cure.

RESULTS OF TREATMENT

A. *Sulfanilamide.*—1. Twenty-four patients were treated with sulfanilamide initially, received an average of 41 Gm. of the drug over an average of nine and four-tenths days and averaged twenty-seven and eight-tenths days from admission to clearance by fever therapy.

Fig. 2 (case 1).—One day after fever therapy, Nov. 4, 1938; × 1,000.

2. Three patients, 2 after sulfapyridine reaction, 1 after fever therapy reaction, were given an average of 36.6 Gm. of sulfanilamide and averaged thirty-three and one-third days from admission to clearance.

3. Nineteen patients were treated with sulfanilamide initially, received an average of 39.1 Gm. of the drug over an average period of eight and four-tenths days, were also given urethral irrigations, and averaged fifty-

three and eight-tenths days to clearance. Most of these patients were given irrigations because the response to sulfanilamide therapy was inadequate.

4. Forty-eight patients treated initially with sulfanilamide averaged 200 Gm. of the drug, were sulfanilamide failures, and were treated by other means.

Fig. 3 (case 2).—One day after patient was started on a course of sulfanilamide, Oct. 14, 1938; × 1,000.

Roughly 50 per cent of the patients treated by sulfanilamide initially can be considered to be cured by this drug.

B. *Sulfapyridine.*—1. Thirty-eight patients were treated with sulfapyridine initially, received an average of 24.5 Gm. of the drug over an average period of eight and seven-tenths days and were given clearance in an average of thirty and one-tenth days from admission.

2. Three patients had gross hematuria and renal colic after initial treatment with sulfapyridine with 10, 10 and 17 Gm. of the drug respectively and were treated by other means.

3. Twenty-four patients who had failed to show favorable response to, or to be cured by, adequate sulfanilamide therapy were given an average of 22.3 Gm. of sulfapyridine over an average period of seven and one-tenth days and were given clearance in an average of forty and eight-tenths days from admission.

4. Thirteen patients who had failed to be cured on adequate sulfanilamide therapy were given an average of 47 Gm. of sulfapyridine, failed to be cured by this drug and were treated by other means.

All of the 38 patients treated initially with sulfapyridine were cured by this drug.

C. *Fever Therapy.*—1. Forty-four patients received an average of one and eight-tenths fever treatments, with an average total of ten and seven-tenths hours at 106.8 to 107 F. and were cured of their gonorrhea.

2. Three patients received an average of two treatments with an average total of eleven and four-tenths hours and were not cured by this treatment. All three refused further fever therapy.

3. Fever therapy of 34 patients was attempted, but an adequate amount of fever could not be given because of complications. Almost all of these patients had had previous unsuccessful sulfanilamide therapy.

D. *Additional Treatment.*—Twenty-three patients, of whom 12 had received adequate sulfanilamide therapy and 11 of whom had received both sulfanilamide and sulfapyridine therapy, were given such general treatment measures as irrigations, intravenous hydrochloric acid and the like and finally recovered after long hospitalization.

E. *Failures.*—Of the 178 patients treated, 3 were not cured of their gonorrhea.

The complications of treatment from sulfanilamide have been mainly febrile reactions, except for one severe case of agranulocytic angina and one bilateral sciatic neuritis. With sulfapyridine, 3 cases of gross hematuria with renal colic occurred. The complications of fever therapy occurring in those who have had sulfanilamide are at least five times as frequent and much more dangerous to life than in those who have not had sulfanilamide. The administration of oxygen is of great worth in these cases and in the event of complication is life saving. The chief complication is cerebral edema, which is thought due to anoxia of the brain tissue, which is in turn thought due to decreased oxygen carrying capacity of the blood. The altitude in Denver is no help, and when, as often occurs, the patient has been transferred to this hospital from a much lower altitude, the difficulties of administering fever therapy with safety are enormous. There were no deaths from complications.

ILLUSTRATIVE CASES

CASE 1.—Six and one-half hours of fever therapy were given on Nov. 3, 1938. The fever was terminated at that amount because of impending cerebral edema. As is our practice when a good start has been made on fever, the patient was prepared for another session the next morning, but a smear was taken just before his being placed in the Kettering hypertherm. Since he showed the good response illustrated in figure 2, this second session of course was not given. Finally, the only cellular elements to be found were a few scattered epithelial cells. Most of the cells were necrosed by karyolysis, but in figure 2 karyorrhexis is evident.

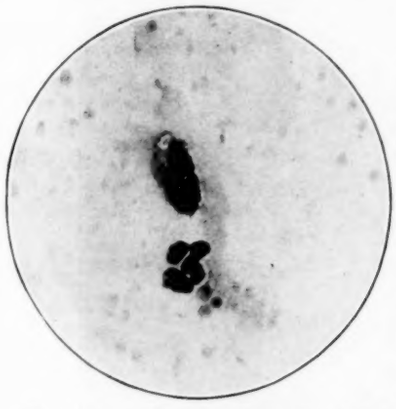

Fig. 4 (case 2).—Nine days after initial dose of sulfanilamide, Oct. 21, 1938; × 1,000.

CASE 2.—This illustrates an ideal response to sulfanilamide medication initially. In figure 3 is seen a very satisfactory smear response even though it is loaded with gonococci. The pus cells show a fragmenting, and no fresh cells are seen. Sulfanilamide was started on Oct. 13, 1938. With the appearance of the smear in figure 3 one can be almost certain that this patient will be cured by sulfanilamide alone, and this excellent result, as seen in figure 4, is as expected.

CASE 3.—Repeated courses of sulfanilamide were administered, with a total in excess of 135 Gm. The prostatic smears were unsatisfactory; a small amount of fresh new pus cells occurring in clumps was continually in evidence. Figure 5 represents one of two such clumps found on the January 24 smear. Careful scrutiny of the January 24 smear revealed

one diplococcus, which was hardly diagnostic. Factually this diplococcus was interesting only, because it was otherwise evident that the patient required other treatment. After several abortive attempts at fever therapy which were abruptly and dramatically terminated by the cerebral edema which so often occurs in those who have had sulfanilamide, one ten hour

Fig. 5 (case 3).—Prostatic smear, Jan. 24, 1939. Note diplococcus; × 1,000.

fever treatment was administered on Feb. 7, 1939. The response to fever therapy, as shown in figure 6, indicates that our belief that the patient was not cured by sulfanilamide was justified. Figure 6 is a low power photomicrograph of a smear that is made very thick to show the almost complete absence of cellular elements in the smear.

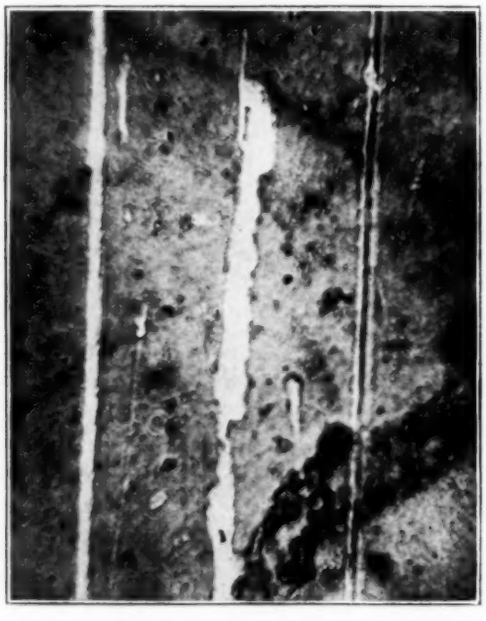

Fig. 6 (case 3).—Nine days after fever therapy; × 100.

COMMENT

From studying and treating these 178 patients with gonorrhea we have gained certain impressions:

1. With sulfanilamide, about half the patients will show an immediate adequate response and will be cured. The other half will show an inadequate response, although there will be great clinical improvement, and these patients should be treated by other means.

2. With sulfapyridine it appears that the immediate adequate response is greater than with sulfanilamide. Sulfapyridine therapy in sulfanilamide resistant cases is very efficacious. In gonorrheal epididymitis and arthritis the response to sulfapyridine therapy is much better than to sulfanilamide.

3. Fever therapy is the most efficacious treatment for gonorrhea but has definite disadvantages in that the treatment is expensive and of danger to the patient. The danger is increased by the previous medication with sulfanilamide, especially since now almost all patients have been so treated before they reach a hospital where fever therapy is available. Fever is of course the standard of good treatment in gonorrheal arthritis. We have had as good therapeutic results with fever therapy by giving eight and a half hours of fever to patients with chronic gonorrhea as with giving ten hours of fever to patients with acute gonorrhea. It has been our habit to give our fever patients a one hour trial treatment. In most cases this has been done on the day before the ten hour treatment, so that a total of eleven hours actually has been given. It is our experience, and thought to be important therapeutically, that if fever therapy for gonorrhea is given in more than one session these sessions should be no further apart than on alternate days.

4. Patients who do not show an adequate response to initial sulfanilamide therapy by the fourth day should be given either fever therapy or sulfapyridine because their chance of attaining a cure from sulfanilamide is not good, hospitalization is increased and the adverse effects of long continued sulfanilamide administration are courted without, in our opinion, therapeutic justification.

5. Estimating the progress of the case to determine effects of therapy, necessity for change in therapy and the time when cure is effected can practicably be accomplished by evaluation of the smear if the doctor in charge of treatment for gonorrhea (*a*) is in control of the staining of urethral and prostatic smears, (*b*) familiarizes himself with the microscopic appearance of necrosing pus cells and (*c*) examines the smears himself. A report of "negative for gonococci" from a laboratory, whether by smear or by culture, means nothing as far as aiding in treatment is concerned. But very specific inferences as to the state of the gonorrheal infection may be drawn from estimating the degree of necrosis in the pus cells of the smear and ascertaining whether or not fresh pus cells are present.

SUMMARY AND CONCLUSIONS

1. One hundred and seventy-eight consecutive patients were treated over a period of twenty-six months by adaptation of a routine treatment to the individual.

2. The criteria of cure presented are not considered to be absolute, not in the class of cultural methods for example, but are criteria which are entirely practicable and have proved to be successful.

3. The increased use of sulfanilamide and sulfapyridine therapy renders fever therapy more difficult to administer and more dangerous to the patient, but to a great extent sulfapyridine has supplanted fever therapy.

4. The method of smear examination and evaluation adopted forms the basis of a practicable therapeutic regimen.

TWENTY MINUTE CARDIAC ARREST WITH COMPLETE RECOVERY

PRINCIPLES OF PREVENTION AND TREATMENT

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Every surgical team will at times be called on to face the serious responsibility of sudden cardiac arrest in the operating room. Such a catastrophe may develop at any point in the procedure—during preliminary preparation, during induction of anesthesia, during the operation or during certain essential postoperative procedures.

The exact physiologic mechanisms involved may be extremely difficult to analyze either at the time or later, after deliberate and full consideration. Prompt, adequate and properly selected methods of stimulating the return of cardiac function, maintaining adequate cerebral oxygenation, are essential in order to save the lives of these patients. However, the exact choice of these procedures and the possibility of their application under the existing circumstances are often difficult. As a result, routine measures and cardiants are applied, frequently without success. Primarily because of this uncertainty in management and results, we have been prompted to report the following case and its discussion, because it represents certain unusual aspects of this problem and has changed some of our fundamental concepts regarding cardiac resuscitation.

REPORT OF CASE

A man aged 20 was first seen at the Lahey Clinic on July 1, 1941 with a history of chronic cough and hemoptysis of four years' duration. Complete studies showed a bronchiectasis of the left lower lobe and spontaneous pneumothorax on this side. Otherwise his examination was essentially negative.

The patient was admitted to the New England Deaconess Hospital on Sept. 26, 1941 for lobectomy. On the fifth day he was prepared for operation. Preoperative blood pressure was 124 mm. systolic and 60 mm. diastolic, the pulse rate 88, the respiratory rate 24. Premedication consisted of 1/6 grain (0.01 Gm.) of morphine, 1/150 grain (0.0004 Gm.) of scopolamine subcutaneously and 1½ grains (0.1 Gm.) of pentobarbital sodium by mouth, given at 12:30 p. m.

At 1:20 a 10 mm. flexible metal endotracheal catheter with balloon cuff was introduced into the trachea under direct vision after topical anesthesia with 10 per cent cocaine hydrochloride. General anesthesia was started at 1:23. The anesthetic mixture for induction was approximately 30 per cent cyclopropane and 70 per cent oxygen in a closed circuit with carbon dioxide absorption. The blood pressure rose to 160 mm. systolic and 100 mm. diastolic; the pulse rate was 72 and the respiratory rate 22. After induction, the balloon cuff was inflated to insure a closed system. The endotracheal tube was connected to the conduits of the gas machine by means of adapters. Anesthesia was then maintained by a mixture of approximately 20 per cent cyclopropane in oxygen.

The operation was started at 1:55 and the thoracic cavity opened at 2:17. At this point the blood pressure was 140 mm. systolic and 96 mm. diastolic, the pulse rate was 104 and the respirations were very shallow and rapid. Periods of passive positive respiration of one to two minutes were resorted to at five minute intervals in order to insure an adequate oxygen-carbon dioxide exchange. The blood pressure and pulse continued at about the same level and were never lower than the preoperative level. At 3:15 the bronchus and vessels leading to the left lower lobe were ligated, the specimen was removed and the stump was sutured and inspected. At 3:25 p. m., two hours after the start of anesthesia, it was decided to aspirate a small quantity of secretion in the trachea through the endotracheal tube. At this time the blood pressure was 140 mm. systolic and 100 mm. diastolic, and the pulse rate was 108. The operative procedures were halted during this interval to permit aspiration, and the surgical team, watching the upper lung and heart, was prepared to prevent possible trauma to the remaining lung tissue if the patient should suddenly cough or strain. After the apparatus for anesthesia was disconnected at the mouth and a number 14 French catheter was introduced through the endotracheal tube for suction, the patient gave three convulsive coughs. At this point the surgeon remarked that the heart had ceased beating and was semidilated and tense. Rhythmic cardiac compression simulating systole was instituted immediately and the patient was put in 5 degree Trendelenburg position. At 3:28, three minutes after cessation, 2 minims (0.12 cc.) of neosynephrin hydrochloride was injected into the musculature of the ventricle; at 3:29 an additional 2 minims of neosynephrin hydrochloride was given into the ventricle and artificial systole was continued. At 3:30, five minutes after cessation, 10 minims (0.6 cc.) of 1:1,000 epinephrine hydrochloride solution was injected, half into muscle and half into the ventricular cavity. The heart began to show fibrillatory movements and then gradually to beat vigorously for five to six beats. It again relapsed into fibrillation and then stopped. A second dose of 1 cc. of epinephrine was introduced, without effect. Actual cardiac compression simulating systole was continued until twenty minutes later, when the heart again began spontaneous rhythmic contractions, at 3:45. At 3:48 p. m. 7 cc. of nikethamide was given into the vein of the foot.

At the instant of cessation of the heart beat all anesthetic gases were discontinued and artificial respiration (28 to 32 a minute) was begun and maintained by strong rhythmic pressure (12 to 16 mm. of mercury) on the rebreathing bag, with only oxygen flowing. At 3:40 p. m., fifteen minutes after cessation, 15 cc. of procaine hydrochloride was adminstered intramuscularly into the left shoulder. Throughout this procedure the patient was cyanotic and the color of his head and shoulders was violescent, but he did not have the grayish, waxy appearance of death. Within a few seconds after the heart resumed spontaneous rhythmic contractions (3:45 p. m.) spontaneous respiratory excursions progressed from rapid shallow respirations to rapid (36 a minute) exaggerated respirations. At 3:50, or twenty-five minutes after cessation of the heart, the patient's color became a livid pink. The blood pressure was first obtained at this time; it measured 160 mm. systolic and 120 mm. diastolic, and the pulse rate was 118. Respirations gradually quieted as to excursion and rate. For the remainder of the operation only oxygen was administered.

Closure of the chest was accomplished in the ordinary manner, and the operation was concluded at 4:50 p. m., one hour and twenty-five minutes after initial cardiac cessation. The operative time was three hours. At this time the blood pressure was 114 mm. systolic and 64 mm. diastolic; the pulse rate was 124. The patient was returned to a private room at 5:10, after he responded to spoken commands, and with the second of two 500 cc. transfusions running. He was placed in an oxygen tent immediately, and the bed was placed in shock position.

Preoperatively a continuous intravenous drip had been started through a gold cannula to the right long saphenous vein at the ankle, and during operation the patient received two transfusions of 500 cc. each. Immediately after operation it was noted that there was no pulse in the right radial artery, but after one hour the pulse in the right arm had returned to its normal magnitude. The operative position, with the right arm dependent, possibly was a factor in the production of this prolonged arterial spasm.

SUMMARY OF POSTOPERATIVE CONVALESCENCE

The patient's immediate postoperative recovery was entirely satisfactory and differed but little from the average lobectomy case. He was mentally clear and alert, and there were no signs of cerebral damage demonstrable at any time. The upper lobe was well aerated and expanded from the beginning, but, because he had a low grade fever, closed drainage was maintained for two weeks and simply converted into open drainage through

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the same tube at the end of the second week. His low grade fever gradually subsided and, since his condition was good, he was allowed to be up on his seventeenth day. On his second day up he complained of persistent frontal headache and his temperature rose to 103 F. He was put back to bed and a course of sulfathiazole was started. Our immediate consideration was the possibility of brain damage and brain abscess. He was seen by the neurosurgical department, which found no abnormal neurologic signs and a lumbar puncture was negative in every respect. Preoperatively he was known to have a chronic pansinusitis, and this was reviewed by our nose and throat consultant and did not seem to be the source of his systemic reaction. He continued to have high temperature, his headache subsided after a few days and he complained of no symptoms whatever thereafter. The continued chemotherapy had no effect on this temperature. Roentgenograms of his chest showed a well expanded upper lobe and no demonstrable pleural infection. Repeated thoracentesis produced no pus. However, because of his continued fever a rib resection was done, establishing more adequate drainage and removing a small amount of fibrin lying along the posterior gutter. This did not affect his temperature, which continued swinging for several more weeks and gradually subsided. During all this time he had no symptoms and felt well. During his convalescence he had two electrocardiograms which were entirely normal, and before discharge from the hospital an electroencephalogram was also made, which was normal. He left the hospital in good condition sixty days after operation.

COMMENT

Discussion of this case may be subdivided into three physiologic divisions. First, what were the etiologic factors causing this cessation? Second, what was the rationale of the treatment employed in this case? Third, what preparation and regimen of treatment might be of value (1) to prevent or (2) to treat a similar condition more adequately if it should arise in the future?

Etiology.—Etiologic factors which might cause this sudden cardiac arrest are (1) idiosyncrasy to the anesthetic drug, (2) onset of ventricular fibrillation, (3) occurrence of a vagovagal reflex resulting in cardiac arrest. Idiosyncrasy to the agent, while possible, is not probable in view of the time of occurrence; that is, two hours after the start of its administration. The onset of ventricular fibrillation can be ruled out, as the surgical team was watching the exposed heart and did not note any fibrillatory movement when massage was started.

In this instance cessation was most likely the result of a vagovagal reflex influenced by the following factors and facts: With the wearing off or loss of topical anesthesia (cocaine) after two hours of operating, vagal irritability returned to this region. Also an increase in the excitability of the vagus fibers resulted from the depression of the cells of the medullary center. The factors influencing this depression were medication, anesthesia and suboxygenation resulting from surgical diminution of vital capacity, as evidenced by the shallow respirations. Stimulation of the vagovagal reflex resulting in cardiac arrest was initiated when the suction catheter irritated or stimulated the irritable tracheal bifurcation, as evidenced by the cough spasm noted just prior to cardiac cessation. Although this reflex may have been transitory, the effect, inhibition or cessation, persisted.

A summation of physiologic factors which may be applicable to this case is found in the chapter on "Physiology of the Heart," of Starling's "Human Physiology."[1] These factors are (*a*) the increase in excitability of the vagus, (*b*) the site of vagal action on the heart, (*c*) vagal mode of action and drugs influencing it and (*d*) the effect of narcosis and anesthesia on vagal action. These factors are more or less explained in the following quotations from "Human Physiology":

A. It is remarkable that the excitability of the vagus fibers is dependent on the condition of the cells of the medullary centers. Thus, if the centers are depressed by narcotics, the vagus fibers become more excitable.

B. The action of the vagus fibers on the heart is almost identical in frog and mammal and is exerted primarily on the auricle. . . . Generally, the vagus absolutely stops the action of all parts of the auricles; in such cases the ventricles also cease beating.

C. Many facts point to the inhibitory impulses acting on the heart muscle itself. . . . These nerve effects are paralyzed by atropine, after administration of which no inhibitory effects can be produced by stimulation of nerve or muscle on any part of the heart. . . . Although various views as to the nature of inhibition have been put forward from time to time, the present tendency is to ascribe both the excitatory and the inhibitory effects of all nervous stimulation to the liberation, at the nerve ending, of small amounts of highly active substances, which are quickly destroyed in the tissues. According to Loewi, the vagus acts by producing some chemical substance which has the power of depressing the activity of the different parts of the heart. . . . It is now generally accepted that this substance is acetyl choline. . . . The action of acetyl choline is antagonized by atropine.

D. When the arterial system is dilated, so that the mean systemic pressure during cardiac inhibition is low, or when the asphyxial gasps of the animal are prevented by anesthesia or by a section of the spinal cord, the heart may fail to recover from the inhibition produced even by transitory stimulation of the vagus. In such cases it is necessary to knead the heart in order to restore its rhythmic action.

Rationale of Treatment in This Case.—The rationale of treatment in this instance was governed more by urgency and expediency than by any prepared plan or organized regimen for treatment.

Artificial systole to maintain circulation was immediately started by the surgeon. The patient was placed in 5 degree Trendelenburg position to facilitate cerebral circulation. Neosynephrin, a synthetic product, was used initially as the pressor stimulant because cyclopropane was the anesthetic agent. Laboratory and clinical reports [2] have demonstrated an increase in irritability of cardiac muscle, with a tendency to ventricular fibrillation when epinephrine is employed as a pressor substance in the presence of tissue saturation with cyclopropane. Procaine was given, with the hope of neutralizing this sensitization.[3] When no effect was obtained from the second injection of neosynephrin, epinephrine then was used. Although this first injection of epinephrine initiated spontaneous cardiac activity, this action rapidly progressed to the undesirable state of ventricular fibrillation to cessation. A second dose of 1 cc. of epinephrine had no effect. Artificial systole was reestablished during fibrillation and subsequent cessation. The heart resumed spontaneous rhythm twenty minutes after the initial cessation. The stimulus undoubtedly was the rhythmic compression of the heart during artificial systole.

Simultaneously, artificial respiration was continued throughout this twenty minute period to maintain adequate pulmonary ventilation. In the absence of mechanical apparatus as recommended by Crafoord,[4]

1. Starling, E. H.: Human Physiology, chapter 31, Physiology of the Heart, ed. 7, Philadelphia, Lea & Febiger, 1936, pp. 734-738.

2. Meek, W. J.; Hathaway, H. R., and Orth, O. S.: The Effects of Ether, Chloroform and Cyclopropane on Cardiac Automaticity, J. Pharmacol. & Exper. Therap. **61**: 240-252 (Nov.) 1937.

3. Burstein, C. L., and Marangoni, B. A.: Protecting Action of Procaine Against Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia, Proc. Soc. Exper. Biol. & Med. **43**: 210-212 (Jan.) 1940.

4. Crafoord, Clarence: Pulmonary Ventilation and Anesthesia in Major Chest Surgery, J. Thoracic Surg. **9**: 237-253 (Feb.) 1940.

Mautz [5] and Beck,[6] the anesthetist immediately started and maintained artificial respiration (28 to 32 per minute) by rhythmic pressure (12 to 16 mm. of mercury) on the rebreathing bag of the gas machine. The anesthetic mixture was immediately replaced by oxygen in the breathing circuit. Oxygen under pressure was supplied to the pulmonary tree by this system of endotracheal tube with inflated cuff, adapter and gas machine. This method resulted in demonstrable, adequate expansion of the lung. The endotracheal tube insured a patent airway. This type of closed system of endotracheal tube with inflated cuff and adapter safeguards against simultaneous, undesirable inflation or acute dilatation of the stomach, which can readily occur when a mask is employed over the mouth and nostrils and strong positive pressure is used. Nikethamide was administered intravenously as a stimulant after the return of circulation and respiration because of its mildly cardiac and pronounced respiratory effect.

Artificial cardiac diastole was most likely produced by the following factors: 1. The inherent elasticity and muscle recoil facilitated auricular and ventricular filling. 2. The intermittent changes in positive pressure exerted during artificial respiration resulted in differences in venous pressure both in the vena cava and in the pulmonary circulation. Exaggerated pulmonary ventilation facilitated blood flow to the auricle from the lungs. The definite discernible artificial diastole probably was dependent on these factors.

During this twenty minute interval, oxygenation was maintained by artificial respiration and circulation. Beck stresses the importance of oxygenation to prevent cellular damage and especially medullary cell damage, with respiratory death. The prevailing impression is that cortical cells begin showing cellular degeneration in the form of tryoidolysis five to seven minutes after being deprived of oxygen. Beck mentions animal experimentation by Weinberger,[7] placing this time at three to five minutes. The lack of progressive signs of anoxia was the motivating influence in the continuation of manual oxygenation over the twenty minute period until circulation and respiration resumed normal activity.

RECOMMENDED METHODS OF PREVENTION AND TREATMENT

Obviously the best management of this problem is its prevention. This necessitates an attempt to avoid the onset of this inhibitory action of the vagus on the heart. This is accomplished first by prevention of increased vagal irritability resulting from suboxygenation or depressing effects of narcosis or anesthesia and second by the prevention of afferent reflexes, or vagovagal reflexes, providing the inhibitory efferent effect. The latter is accomplished by avoiding or blocking, whenever possible, stimuli affecting the afferent pathways of the vagal nerve. It is our opinion that necessary procedures, such as aspiration of trachea and hilar manipulations, which may produce afferent vagal stimulation, should not be carried out without adequate block of these pathways. Local infiltration of hilar plexes or topical application of anesthetic to the tracheobronchial tree should afford some protection. In addition, the efferent effects of the vagus nerve are blocked directly at the myoneural junction by an adequate dose of atropine. Atropine $\frac{1}{75}$ grain (0.0008 Gm.) is considered by many to be an adequate dose. This can be given as part of the preoperative medication and repeated as indicated, depending on the duration of the operation.

However, when this catastrophe occurs, the following plan of treatment is recommended. Adequate tissue oxygenation by means of artificial circulation and pulmonary ventilation should be instituted immediately and simultaneously. This is accomplished by the following methods:

Artificial Respiration.—An endotracheal tube, preferably with a balloon cuff attachment, should be inserted to insure a patent airway. Inflation of the balloon cuff insures a closed system with the distribution of the positive pressure within the pulmonary tree only. In the absence of apparatus to produce intermittent positive pressure (Mautz), rhythmic pressure on the rebreathing bag of the closed circuit will insure adequate pulmonary ventilation. Carbon dioxide absorption is essential to prevent accumulation of this product within the closed system. Rhythmic pressure of 12 to 16 mm. of mercury at a rate of 28 to 32 per minute is recommended.

Artificial Circulation.—Circulation of the blood should be maintained by artificial systole in the form of rhythmic manual compression. It is advisable to synchronize this rhythm with that of artificial respiration to allow for the associated artificial diastole. This necessitates cardiac accessibility.

If the chest is open, the pericardium can be opened from either side and an efficient artificial systole instituted. If the abdomen is open, the approach may be made through the left diaphragm. If neither chest nor abdomen is open at the time, a rapid exposure of the heart can be accomplished by an intercostal incision in the anterolateral portion of the left chest, cutting the costal cartilage above and below. The influence of gravity on the cerebral circulation should be considered. A few degrees of Trendelenburg is a factor in aiding cerebral circulation.

Cardiants may be used in physiologic doses. Although their use is a standard method of treatment, many untoward and fatal effects have been observed. It is our opinion that the best treatment combines the outlined recommendations and the very judicious use of cardiants.

CONCLUSIONS

1. This case demonstrates that the time interval of cardiac arrest compatible with normal recovery is much longer than was formerly appreciated.
2. This recovery is dependent on adequate tissue oxygenation, especially of cerebral tissue.
3. This is accomplished by immediate and simultaneous artificial circulation and respiration.
4. Efficient artificial circulation is dependent on more than simple cardiac massage.
5. The measures instituted must approach as closely as possible the normal physiologic cardiorespiratory sequence.
6. Synchronized artificial respiration associated with artificial cardiac diastole followed by artificial cardiac systole more nearly approaches this normal sequence.
7. This case with complete recovery following prolonged cardiac arrest demonstrates the value of these principles of prevention and treatment.

605 Commonwealth Avenue.

5. Mautz, F. R.: A Mechanical Respirator as an Adjunct to Closed System Anesthesia, Proc. Soc. Exper. Biol. & Med. **42**: 190-192 (Oct.) 1939.

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Clinical Notes, Suggestions and New Instruments

LARYNGEAL STRIDOR ASSOCIATED WITH HYPOCALCEMIA IN AN ADULT

POSTOPERATIVE PARATHYROID DEFICIENCY WITH OTHER CONTRIBUTING ABNORMALITIES

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Laryngeal spasm as a symptom of tetany in infancy is well recognized. In later life it is rarely encountered. Guild [1] states that it almost never occurs after the second year. The following report of laryngeal stridor associated with parathyroid tetany indicates that under certain circumstances the symptom does occur in adult life. A Jewish housewife aged 70 had a bilateral thyroidectomy performed for colloid goiter when she was 47. At 60 she had a bilateral iridectomy done for cataracts; at 63 she began to notice the onset of hoarseness, at 64 the initial phase of chronic congestive heart failure and at 69 acute attacks of laryngeal stridor. The Chvostek and Trousseau signs were positive; the serum calcium was found to be 4.2 mg. per hundred cubic centimeters, and the attacks of stridor were instantly relieved by intravenous calcium gluconate. Control of the serum calcium level with dihydrotachysterol relieved the symptom.

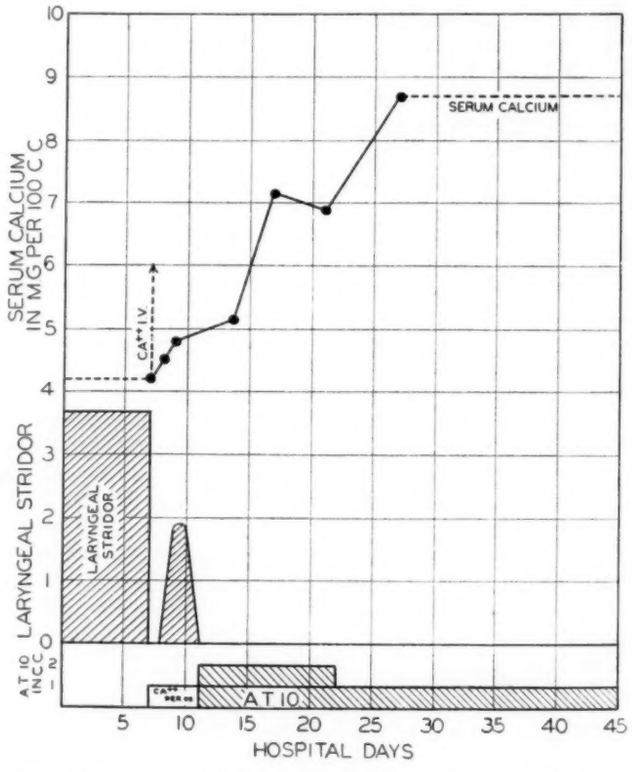
Albright [2] reports that he now has under observation a similar case. In his case the laryngeal stridor also developed many years after thyroidectomy, at a time of physical disability and in association with a paralyzed vocal cord. His patient, however, has not responded so definitely to treatment with dihydrotachysterol.

REPORT OF CASE

History.—G. S., Jewish housewife aged 70, was essentially well until she was 47 (1917), at which time a colloid adenoma of the thyroid was removed. The postoperative chart indicates an uneventful convalescence. Ten years later the onset of bilateral lenticular opacities was observed and three years subsequently, at the age of 60 (1930), iridectomies were performed. At 63 (1933) she first began to notice increasing hoarseness, and one year later she commenced to suffer from prolonged periods of edema of the ankles. The edema was successfully treated by her private physician with digitalis, diuretics and rest. At 66 (1936) she noticed her first attacks of laryngeal spasm with inspiratory crowing respiration. These occurred at intervals of several weeks and were usually precipitated by emotional tension, particularly by anger. The attacks occurred with gradually increasing frequency until she was 69 (1940), at which time they became much more prolonged and occurred independently of emotional stress. She became cyanotic during the attacks. Six months before admission she became so weak that she could seldom go out, and increasing dyspnea and orthopnea developed. These symptoms and her stridulous breathing became worse until the time of admission.

Examination.—On physical examination the patient was pale, senile and chronically ill and lay propped up in bed in constant mild dyspnea. Basic respiration was regular. At times, however, she was seized with sudden attacks of crowing inspiratory stridor which would last for from two to three minutes. In the more severe attacks deep cyanosis would develop, producing a clinical picture that was truly alarming. The skin was not remarkable. The eyes showed the scars of iridectomy. A scar of the thyroidectomy was present. There was moderate distention and pulsation of the veins of the neck. The heart was clinically enlarged. The heart sounds were regular, of a ticktack quality, with a soft blowing apical systolic murmur. The blood pressure was 127 systolic and 68 diastolic. The radial arteries were palpable. There were coarse rales at the bases of both lungs. The abdomen was distended, with fulness in the flanks, shifting dulness and a fluid wave. There was pitting edema of the abdominal wall and of the lower extremities. Laryngoscopic examination revealed paralysis of the right vocal cord.

Repeated examinations of the urine revealed a specific gravity varying from 1.010 to 1.025, traces of albumin but no sugar. There were small numbers of white blood corpuscles and rare hyaline and fine granular casts in the sediment. On admission the hemoglobin content was 65 per cent (Hayden-Hausser), the red blood cell count 4,370,000 and the white blood cell count 9,250. The stained smear showed adequate platelets and moderate achromia. The differential count showed 89 per cent polymorphonuclears, 7 per cent lymphocytes and 4 per cent large mononuclear cells. The nonprotein nitrogen was 35 mg. per hundred cubic centimeters, the total serum protein 8.4 Gm., serum phosphorus 4.3 mg. and serum alkaline phosphatase activity 4.6 Bodansky units. Serum calcium determinations on three successive days were 4.2, 4.5 and 4.8 mg. per hundred cubic centimeters. (The latter two readings followed calcium administration.) Stool examinations were negative for occult blood. A phenolsulfonphthalein renal function test showed 19 per cent excretion of dye at the end of one hour. Roentgen examination of the long bones, skull and spine showed moderate demineralization of the lumbar spine.



The abscissa illustrates the serum calcium level in milligrams per hundred cubic centimeters and the disappearance of laryngeal stridor, and at the bottom of the chart is given the dosage of dihydrotachysterol (A. T. 10). The ordinate represents time in hospital days. Note that following the administration of dihydrotachysterol the blood calcium level rapidly rose in association with continued relief of the laryngeal spasm.

Hospital Course.—Although the cardiac reserve was obviously very limited, there was considerable improvement in dyspnea and edema as the result of bed care, thoracenteses, diuretics and digitalization. This improvement did not, however, appear to influence the periods of inspiratory laryngeal stridor, which occurred many times a day, lasted for several minutes and at times were accompanied by an alarming degree of cyanosis. At the time of these attacks the Trousseau sign was definitely positive and the Chvostek sign slightly positive.

On the seventh hospital day 1 Gm. of calcium gluconate was administered intravenously during a seizure, with immediate

From the Medical Department, Hartford Hospital.

1. Guild, H. L., in Practice of Pediatrics, edited by Joseph Brennemann, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 1, chapt. 37.

2. Albright, Fuller: Personal communication to the author.

relief that persisted for about twenty hours (shown in the chart). In view of the instant response to intravenous injection, 3 Gm. of calcium gluconate and 1 cc. of percomorph oil were administered daily by mouth. This regimen was associated with a slight elevation of serum calcium (from 4.2 to 4.8 mg. per hundred cubic centimeters) and with partial alleviation of respiratory stridor. On the eleventh hospital day this regimen was supplemented with dihydrotachysterol, which was given in doses of 2 cc. daily for a period of eleven days and in doses of 1 cc. daily thereafter.

During the eleven day period in which 2 cc. of dihydrotachysterol was given, the serum calcium rose from approximately 5 mg. to approximately 7 mg. per hundred cubic centimeters, and the respiratory stridor disappeared entirely and permanently. During the first six days after reduction of the daily dose to 1 cc. the serum calcium continued to rise, attaining the level of 8.7 mg. per hundred cubic centimeters on the twenty-seventh hospital day.

After the twenty-seventh hospital day serum calcium determinations were discontinued, and the dosage of dihydrotachysterol was regulated by means of urinary calcium. This was crudely determined by means of the Sulkowitch test.[3] Observations were made on the twenty-fourth, twenty-fifth, thirty-second and thirty-fourth hospital days, at which times a "moderate amount" of calcium was present. This indicates satisfactory dosage.

COMMENT

The serum calcium level of 4.2 mg. per hundred cubic centimeters is extremely low. If this degree of hypocalcemia had developed suddenly after the thyroidectomy at the age of 47, death would almost certainly have ensued, yet the postoperative course at that time appears to have been uneventful. One must conclude that the hypocalcemia developed gradually. The development of cataracts suggests that it was well established by the age of 57. The reason for this gradual development of hypocalcemia is not clear. Retention of phosphorus caused by severe renal failure is known to produce hypocalcemia in some instances.[4] In this case there was impaired excretion of the dye but no evidence of retention of nitrogen or phosphorus. This explanation is therefore inapplicable. Hypoproteinemia is usually associated with a mild degree of hypocalcemia, but in this case the serum protein was normal. A third possible explanation is that one or more parathyroid glands were left in situ at the time of operation and subsequently atrophied. Such residual tissue or its vascular supply might well have become involved in an area of scar tissue and gradually strangulated. A less conventional hypothesis is that fatigue atrophy, such as the hydropic degeneration of islet tissue observed by Allen[5] in partially pancreatectomized dogs, may have occurred. The production of such atrophy by continued administration of anterior pituitary extracts and its prevention by adequate insulin dosage have led Haist, Campbell and Best[6] to certain observations on the possible prevention of diabetes mellitus.

No more clear is the reason why symptoms of laryngeal stridor should have made their appearance so late in life. The paralyzed vocal cord was undoubtedly present immediately after the thyroid operation, and there is evidence from the lenticular opacities that a certain degree of hypocalcemia also preceded the onset of stridor. Chronologically the onset of stridor was associated with the onset of chronic myocardial failure. All these factors are probably important, and their coincident occurrence probably explains the rather bizarre phenomenon of laryngeal stridor as a symptom of hypocalcemia in an adult.

3. Albright, Fuller: Note on the Management of Hypoparathyroidism with Dihydrotachysterol, J. A. M. A. **112:** 2592-2593 (June 24) 1939.

4. Albright, Fuller; Drake, T. G., and Sulkowitch, H. W.: Renal Osteitis Fibrosa Cystica, Bull. John Hopkins Hosp. **60:** 377-399 (June) 1937. Albright.[3]

5. Allen, F. M.: Experimental Studies in Diabetes: Series 14. The Pathology of Diabetes: 4. The Role of Hyperglycemia in the Production of Hydropic Degeneration of Islands, J. Metabolic Research **1:** 75-88 (Jan.) 1922.

6. Haist, R. E.; Campbell, James, and Best, C. H.: The Prevention of Diabetes, New England J. Med. **223:** 607-615 (Oct. 17) 1940.

SUMMARY

A woman with paroxysmal laryngeal stridor associated with hypocalcemia was treated with dihydrotachysterol. Elevation of the serum calcium level resulted in complete disappearance of the paroxysms. The symptoms developed long after the thyroid gland had been surgically removed. A paralyzed vocal cord and the gradual onset of chronic myocardial failure were complicating abnormalities which presumably played a role in the development of the syndrome, one which though common in infancy almost never occurs in adult life.

179 Allyn Street.

PYOURETER SEVENTEEN YEARS AFTER NEPHRECTOMY

SELVAN DAVISON, M.D., NEW YORK

The occurrence of pyoureter many years after nephrectomy without complete removal of the corresponding ureter is not common. In the case here presented the clinical picture caused by pyoureter was characterized mainly by obscure fever of six weeks' duration.

REPORT OF CASE

History.—R. W., a woman aged 53 born in Russia had had rheumatic fever in childhood. A right mastoidectomy was performed thirty years before the present admission. An appendectomy was done five years later, followed in two weeks by a right ureterolithotomy. Eight years later a right nephrectomy for calculus pyonephrosis was performed at another hospital. For many years, until four years ago, the patient had attacks of cramping pain in the right upper quadrant of the abdomen brought on by food and relieved instantly by licorice powders. Eight years before this admission she was told that she had gallstones but refused operation. During the last seventeen years, there were no genitourinary symptoms. Dysuria, hematuria, frequency, urgency and attacks of renal colic had been completely absent. The menopause occurred at the age of 49.

Six weeks before admission the patient was suddenly seized with sharp pain in the right lower quadrant of the abdomen and had a temperature of 102 to 103 F. for several days. She then was out of bed, although the pain persisted and numerous chilly sensations occurred. For six weeks she complained of moderate generalized malaise. The day before admission, the pain and chilly sensations increased noticeably, and the temperature was 102.5 F. The patient was then admitted to the hospital.

Examination.—The patient had a sallow complexion. She was not in acute distress. A loud systolic murmur was heard all over the precordium and was heard best at the pulmonic area. The second pulmonic sound was greater than the second aortic sound. The blood pressure was 120 systolic and 75 diastolic. There was well defined tenderness in the right lower quadrant of the abdomen and a sensation of fulness in the upper part of that area. On pelvic examination the right fornix was felt to be full and boggy, and there was a definite sensation of thickening and induration in the region of the right broad ligament. Rectal examination gave essentially negative results. The chest was clear. Icterus was not noted.

The urine on admission was essentially normal. After several days a few white blood cells were noted. The first urine culture showed Streptococcus hemolyticus alpha. Two weeks later a second urine culture revealed Staphylococcus aureus beta and diphtheroids. On two examinations no acid-fast bacilli were found in urines taken with the cystoscope. Blood culture on admission showed Staphylococcus aureus alpha in three flasks. The hemoglobin content was 83 per cent and the white blood count was 13,250 per cubic millimeter, of which 58 per cent were segmented polymorphonuclear cells and 2 per cent nonsegmented; there were 28 per cent lymphocytes and 12 per cent monocytes. The blood urea nitrogen

From the Medical Service of Dr. George Baehr, Mount Sinai Hospital.

was 10 mm. per hundred cubic centimeters, the icteric index was 6, the cholesterol was 190 mg., the blood Wassermann reaction was negative and blood agglutination tests for typhoid, infectious mononucleosis and undulant fever were negative.

Course.—After several days, because of a positive blood culture, the patient was given sulfathiazole, 1 Gm. every four hours. Chemotherapy was instituted at the time that the temperature was apparently falling spontaneously. The drug had to be discontinued after three days owing to the development of a classic although mild sulfathiazole eruption of the skin. The blood cultures remained sterile subsequent to the first positive report.

The mass in the right lower quadrant of the abdomen was suggested on admission to be due to an abscess in the stump of the right ureter which had not been removed following a nephrectomy seventeen years before. A barium enema was given to rule out the possibility of a neoplasm of the cecum. The barium enema gave negative results, except that three concretions, probably representing gallstones, were seen in the right upper quadrant of the abdomen. An intravenous pyelogram was then done and revealed a well visualized left upper urinary tract with enlargement of the left kidney. Distorted calices were noted, and these gave the appearance of multiple cysts. The left ureter was normal. The right upper urinary tract was not visualized, and the outline of the right kidney was not seen. An ovoid concretion 1.5 cm. in length was seen over the right wing of the sacrum. The relationship of this concretion to the ureter was not demonstrated, although it was reported as probably representing a ureteral calculus. There was a small concretion in the midline of the pelvis overlying the lower sacrum.

The patient's general condition continued to be surprisingly good. There was little spontaneous pain and the temperature ranged around 101 F. Cystoscopy was performed by Dr. Leo Edelman.

Cystoscopic Observations.—Two hundred and fifty cc. of turbid urine was evacuated from the bladder. A low grade cystitis was noted, with mucopus on the floor especially in the region of the right ureteral orifice. The left ureteral orifice was normal, and crystal clear urine was seen coming from the left ureter, into which a catheter was easily introduced. The operator was unable to engage a catheter on the right side and an orifice was not definitely visualized because of inflammation and edema. The margin of the inferior sphincter was slightly elevated and congested. The bladder urine showed frequent white blood cells. Ureteral urines were normal.

Sufficient evidence was now at hand to be certain that a periureteritis and a ureteral abscess were present. Therefore, exploratory laparotomy was performed by Dr. Leo Edelman. The distal remaining 8 inches (20 cm.) of the right ureter was revealed. Intense periureteral inflammation and thickening were present. The proximal portion of the ureteral stump contained a large abscess, and through the proximal opening purulent material was flowing. The distal end of the ureter contained a calculus which blocked the ureteral orifice. The entire remaining 8 inches of the right ureter was excised and a drain left in the operative site.

The postoperative course was slightly rough for four days, during which time there was fever to 105 F. She received sulfathiazole during these four days and the temperature came down sharply to 100 F. The remainder of the postoperative course was essentially uneventful, although moderately slow because of drainage from the wound. The drainage eventually ceased and the patient was discharged cured.

COMMENT

Jeck [1] has said that "given an infected ureter, the corresponding kidney of which has been removed, whether or not the stump will become a pus pocket, depends chiefly on two factors: (1) the presence of an obstruction, such as stone, stricture or kink and (2) injury to the nerve supply of the ureter, either by operative trauma or peri-ureteritis and consequent scar formation."

The presence of a calculus in this case bears out the observation that obstruction is necessary for the formation of a pus pocket. No pathologic process remains in the great majority of cases of nephrectomy, although the ureter or part of it is left in situ. This is due to the fact that adequate drainage of the stump usually occurs. Latchem,[2] in his experimental work on the physiopathology of the ureter, has shown this to be so. His conclusions are: 1. Absorption of the contents of a distended ureter is very limited if it occurs at all. 2. If infection is present in the ureteral contents, it may spread through the ureteral wall and give rise to periureteral infection and abscess formation.

The most interesting fact in the case history is that the patient was symptom free for seventeen years following nephrectomy. Hennessey,[3] in reviewing reports by Roedelius [4] and Brongersma [5] of pyoureter developing seventeen and twenty-three years respectively after nephrectomy, states that the reason was delay in recognition. He believes that the majority of such cases are and should be detected between a period of a few months and three years after nephrectomy. While this is probably true in the majority of cases, the patient here described was symptom free and did not seek a physician's advice for any genitourinary complaints for seventeen years. There was no dysuria and even when she was in the hospital there was no pyuria or hematuria. Consequently, one may postulate the possibility of sudden exacerbation of a latent infection by an unknown cause. Apparently sufficient ureteral contractions occurred [6] to cause spillage of the contents, periureteritis and Staphylococcus aureus bacteremia. In the case just presented, the calculus was far down the ureter and blocked drainage into the bladder. The presence of some inflammation at the right ureteral orifice was probably a concomitant of the severe periureteritis. Since patency of the lower end of the ureter was blocked, infection sought another outlet. This was through the free end of the ureteral stump. One cannot tell when the actual formation of the periureteritis and the abscess took place. It may have been a slow, symptomless process for seventeen years which suddenly lit up. It is possible that for many years the calculus was not causing obstruction, and then shifting its position closed off the exit to the bladder and therefore blocked the natural drainage with consequent formation of an empyema in the stump of the ureter.

I do not intend to discuss treatment except to mention the fact that most writers on the subject such as Hyman, Hunt, Reid, Latchem and White recommend surgical removal of the infected stump. This was carried out in the case reported in this paper.

SUMMARY AND CONCLUSIONS

Pyoureter and periureteritis occurred seventeen years after nephrectomy for calculous pyonephrosis. The stump of the ureter contained a calculus.

No genitourinary or other symptoms referable to the process were present during these seventeen years.

The patient presented a diagnostic problem of obscure fever of six weeks' duration.

Successful surgical removal was carried out.

It is important to determine at the time of nephrectomy whether the ureteral orifice into the bladder will remain patent. If by the presence of a calculus or stricture free drainage into the bladder is prevented, complete ureterectomy should be carried out to obviate future infection and empyema in the ureteral stump.

5 East One Hundred and First Street.

1. Jeck, H. S.: Pyoureter, Surg., Gynec. & Obst. **52**: 1158 (June) 1931.

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6. Fronstein, R.: Das Empyem des Harnleiterstumpfes. Ztschr. f. urol. Chir. **20**: 183, 1926. Latchem.[2]

PSEUDOEPITHELIOMATOUS HYPERPLASIA IN A CASE OF MULTIPLE PYODERMA

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AND M. E. OBERMAYER, M.D., LOS ANGELES

Pseudoepitheliomatous hyperplasia has lately been studied extensively by Winer.[1]. His report covers the literature so completely and reviews the theoretical and practical considerations of this difficult problem so thoroughly that these topics need not be discussed here.

The following case is reported because we believe that it illustrates well the practical difficulties intrinsic in the histologic diagnosis of pseudoepithelioma.

REPORT OF CASE

A. S., a white man of native Kentucky stock, aged 50, complained of ulcers on the buttocks of about six months' duration. The lesions started as small painful "spots" and gradually enlarged to cover the entire left buttock and the adjacent part of the thigh and the medial half of the right buttock. The history that the patient gave must be accepted with reservations, because he frequently changed his story. He spent the greater part of his life in various institutions of correction. When free, he was either a broommaker, a gardener or an itinerant cosmetic peddler. Questioning in regard to venereal diseases brought the reply "Yep, doc. I've had all of them many times, and lots of shots—got yellow from them once—lasted three months." The only other illnesses he remembered were childhood diseases.

Fig. 1.—Section from border of ulcer, showing thickening of the epidermis, disruption of basal cell layer, apparent infiltration of dermis with nests of cells and dermal cellular infiltrate. Low magnification.

His general development and nutrition were good. Examination revealed that the skin of the affected area was erythematous and definitely indurated. Within this area were scattered tender, crusted lesions approximately 1.5 to 2.5 cm. in diameter. Removal of the crusts disclosed ulcers with nonindurated, rolled borders and an uneven, easily bleeding, depressed surface. In addition, small ulcerated lesions of the ecthyma type were present on the elbows and on the anterior surfaces of the ankles and feet.

Fig. 2.—High magnification of figure 1, showing concentric arrangement of cells with keratinized cell types in the center, cellular anaplasia and mitotic figures.

Scattered over the lateral and posterior aspects of the thighs and the anterior portions of the legs were atrophic scars with hyperpigmented borders; their outline was suggestive of healed cutaneous gummas.

A provisional diagnosis of pyoderma, with infectious granuloma of syphilitic or fungous origin as an alternative diagnosis, was made.

The blood count was normal; examination of the blood, including Wassermann, Kahn, Kline and Mazzini tests, gave negative results; the result of the provocative Mazzini test was likewise negative.

Two specimens from the borders of the ulcers were removed for biopsy and examined at the University of Chicago Clinics.

One section showed the features of an infectious granuloma with epidermal proliferation and heavy dermal infiltration, consisting mainly of plasma and epithelial cells, which reached far down into the dermis.

The other section, however, showed the features illustrated in figures 1 and 2. The epidermis was considerably thickened. The basal cell layer was disrupted and the dermis appeared to be infiltrated with nests of cells resembling those of the prickle cell layer. The arrangement of the cells was concentric, with keratinized cell types in the center. Distinct cellular anaplasia was present, and numerous mitotic figures were seen. The dermis appeared to be disrupted and edematous. A cellular infiltrate, composed for the most part of round cells and some plasma cells, was present around the nest of epithelial cells. On the basis of these features a diagnosis of squamous

1. Winer, L. H.: Pseudoepitheliomatous Hyperplasia, Arch. Dermat. & Syph. **42**: 856-867 (Nov.) 1940.

cell carcinoma was made. However, since the history of multiple ulceration of comparatively short standing did not seem in agreement with the histologic diagnosis, the section was shown to Dr. H. Gideon Wells, of the Department of Pathology of the University of Chicago, who confirmed the diagnosis of squamous cell carcinoma.

The incorrectness of the histologic diagnosis was soon brought out by the clinical course of the disorder. The simple local measures employed consisted of sitz baths of a solution of potassium permanganate (1:8,000) several times daily and alternate applications of boric acid ointment, U. S. P., and of a 2 per cent aqueous solution of methylrosaniline. In addition, several iron compounds and liver extract were administered. The ulcers improved slowly but constantly and were almost entirely healed within a period of twenty weeks, at which time the patient was lost from observation.

The nonmalignant character of the ulcers was also verified histologically by a second biopsy, performed eighteen weeks after the first; the specimen was removed from an area practically contiguous to that from which the first specimen was taken. The second section showed none of the features of squamous cell carcinoma but only those of a nonspecific infectious granuloma.

SUMMARY AND CONCLUSIONS

One of the ulcers in a case of multiple pyoderma with pseudoepitheliomatous hyperplasia at biopsy showed features so suggestive of squamous cell carcinoma that a dermatologist and a pathologist independently made that diagnosis. The practical difficulty of recognizing pseudoepitheliomatous hyperplasia histologically is illustrated.

347 West Berry Street—1930 Wilshire Boulevard.

Council on Pharmacy and Chemistry

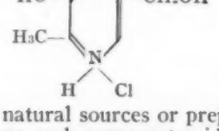
NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

IT SHOULD BE NOTED THAT FOR THE PRESENT THE COUNCIL ACCEPTS PYRIDOXINE HYDROCHLORIDE ONLY FOR PURPOSES OF STANDARDIZATION AND EXPERIMENTATION.

A. E. SMITH, M.D., Acting Secretary.

PYRIDOXINE HYDROCHLORIDE.—2-methyl-3-hydroxy-4,5-*di* (hydroxymethyl) pyridine hydrochloride (vitamin B_6 hydrochloride).—$C_8H_{11}O_3N.HCl$ (205.64). Pyridoxine Hydrochloride has the following structural formula:



It may be isolated from natural sources or prepared synthetically from ethoxy-acetylacetone and cyanoacetamide.

Actions and Uses.—The nutritive and therapeutic value of pyridoxine hydrochloride has not been definitely established. It has been accepted by the Council for purposes of standardization and experimentation only.

Dosage.—A dose of 5 to 10 mg. daily is suggested.

Pyridoxine hydrochloride occurs as a white, odorless, crystalline powder which melts with decomposition between 200 and 212 C. Under the polarizing microscope it appears as thick, birefringent rods and broken fragments. When recrystallized from methanol containing a few drops of concentrated hydrochloric acid, needle-shaped crystals are obtained which are birefringent and exhibit oblique extinction. In the crystalline state it is reasonably stable to light and air. Acidic aqueous solutions of pyridoxine hydrochloride are stable and may be heated for thirty minutes at 120 C. without decomposition. It is soluble in water (22 Gm. per hundred cubic centimeters); slightly soluble in 95 per cent ethanol (1.1 Gm. per hundred cubic centimeters); sparingly soluble in acetone; practically insoluble in ether. Aqueous solutions are acidic (*p*H about 3.0 for a concentration of 10 mg. per cubic centimeter), produce a red color with ferric chloride solution, yield a precipitate with phosphotungstic acid solution and yield a precipitate with silver nitrate solution which is insoluble in nitric acid but soluble in ammonia water.

Dissolve a few crystals of pyridoxine hydrochloride in 2 cc. of alcohol. Add 2 drops of 10 per cent ammonium hydroxide solution and 1 cc. of 2,6-dichloroquinone chloroimide solution (0.01 per cent in alcohol): a deep blue color forms on standing.

Char 0.4 Gm. of pyridoxine hydrochloride. Boil the charred mass with a mixture of 2 cc. of concentrated nitric acid and 8 cc. of water; filter, wash with water, evaporate the filtrate to dryness and dissolve the residue in 0.5 cc. of tenth-normal hydrochloric acid; dilute to 5 cc. with water and add 5 cc. of hydrogen sulfide solution; any color produced does not exceed that of a blank control containing 0.02 mg. of lead (0.005 per cent as lead).

When dried over sulfuric acid, anhydrous calcium sulfate or anhydrous magnesium perchlorate for twenty-four hours, the loss in weight does not exceed 0.2 per cent.

Determine the carbon and hydrogen content by combustion: the carbon content is not less than 46.5 nor more than 46.9 per cent; the hydrogen content is not less than 5.6 nor more than 6.0 per cent. The residue from the carbon-hydrogen determination, or from an ash determination, does not exceed 0.05 per cent.

Determine the nitrogen content: the amount found is not less than 6.6 nor more than 6.9 per cent.

Method of Assay for Tablets and Solutions.

The following reagents are necessary:

1. Veronal Buffer.—Dissolve 18.0 Gm. sodium diethylbarbiturate in 700 cc. of distilled water and titrate with normal hydrochloric acid to a *p*H of 7.5 to 7.7, using a glass electrode. Filter off the precipitate of diethylbarbituric acid. (If the buffer is allowed to stand over twenty-four hours, the *p*H must be readjusted with either normal hydrochloric acid or normal sodium hydroxide to a *p*H of 7.5 to 7.7.)

2. Chloroimide Reagent.—Dissolve 25.0 mg. 2,6 dichloroquinone chloroimide in 100 cc. of acid-free butanol. If the reagent is to be kept for some time, it must be stored in a brown, glass-stoppered bottle at refrigerator temperatures; treated thus, it is stable for about two weeks.

3. Standard Solution.—10.0 mg. of dried crystalline pyridoxine hydrochloride is dissolved in exactly 100 cc. of absolute alcohol. If the solution is to be used immediately, 95 per cent ethanol may be employed. (In the absence of a microbalance, a larger quantity may be weighed and appropriate dilutions made from the more concentrated stock solution.)

Procedure.—Dilute the pyridoxine hydrochloride solutions to be tested to a final concentration in 0.10 mg. of pyridoxine hydrochloride per cubic centimeter. In the case of tablets, a sufficient number—ten or more—are transferred to a volumetric flask, water added and the flask shaken to disintegrate the tablets. After diluting to the mark, the solution is filtered, the first 25 cc. discarded and the next 25 cc. saved for the test.

In the following procedures the preparation of the standard and unknown must be carried on concurrently to allow the same amount of time for the development of color in the two solutions:

Transfer 5.0 cc. of the solution to be tested (after diluting as indicated) to a 50 cc. volumetric flask. Add 5.0 cc. of the veronal buffer and 20 cc. of ethanol.

Prepare a standard comparison solution by transferring 5.0 cc. of the standard pyridoxine hydrochloride solution to a 50 cc. volumetric flask, adding 5.0 cc. of veronal buffer, 15 cc. of ethanol and 5 cc. of water.

Now add to both solutions 5.0 cc. of butanol chloroimide reagent, start timing, and shake intermittently for twenty minutes. Dilute to the mark with ethanol and compare in a colorimeter. The pyridoxine hydrochloride found is not less than 93 or more than 107 per cent.

EVIPAL SOLUBLE.—Evipal sodium.—Sodium N-methyl-cyclohexenyl-methyl-barbiturate.—Sodium 1,5-dimethyl-5-△-1-cyclohexenyl barbiturate.—Sodium cyclohexenyldimethyl barbiturate.—$C_{12}H_{15}O_3N_2Na$. The sodium salt of 1,5-dimethyl-5-$\triangle^1$-cyclohexenyl barbituric acid.

Actions and Uses.—The actions and uses of evipal soluble are essentially similar to those of pentobarbital sodium except that it is designed only for intravenous use to produce anesthesia of short duration. When injected intravenously it is a quick-acting, general anesthetic with an early recovery period. In the majority of cases consciousness is restored in from fifteen to thirty minutes, depending on the amount of drug injected. Not uncommonly there follows some drowsiness or sleep if the patient is left undisturbed. While the intravenous use of barbiturates is a valuable procedure under certain circumstances it should be undertaken only by those experienced in this field who have had special training in the use of anesthetics of this type. It should not be looked on as an office procedure; adequate facilities should be at hand to combat untoward reactions. Ataxia and transient amnesia may occasionally be encountered. Contraindications are in general those of the barbital compounds and general anesthetics.

Dosage.—As there is considerable variation in individual reactivity to any of the barbiturates, the dose must be individualized. In general, 2 cc. to 4 cc. of a 10 per cent solution is required to induce unconsciousness in adults; this is injected intravenously at the rate of 1 cc. per ten seconds. An additional 1 cc. or 2 cc. may be necessary if relaxation is not obtained with the initial dose, or it may be required during the operative procedure. A total amount of 10 cc. of this 10 per cent solution is seldom required for adults, and it cannot be exceeded without danger.

Caution: If the solution is discolored or shows the presence of undissolved particles, even though it is freshly prepared, it should be discarded. The powder and solution undergo change on exposure to air and should not be kept for future use.

Manufactured by Winthrop Chemical Co., New York. U. S. patent 1,947,944. U. S. trademark 315,515.

Ampules Evipal Soluble, 0.5 Gm.: powder, packaged with or without sterile distilled water.

Ampules Evipal Soluble, 1 Gm.: powder, packaged with or without sterile distilled water.

Evipal soluble occurs as a white, crystalline, odorless, hygroscopic powder, with a slightly bitter taste; very soluble in water, freely soluble in alcohol; practically insoluble in ether. An aqueous solution of evipal soluble is alkaline to litmus.

Dissolve about 0.5 Gm. of evipal soluble in 100 cc. of water, add an excess of diluted hydrochloric acid, mix, allow to stand fifteen minutes and collect the resultant cyclohexenyl*di*methyl barbituric acid on a filter, wash with water and dry at 65 C.: it melts at 143-146 C.

Transfer about 0.1 Gm. of the dried cyclohexenyl*di*methyl barbituric acid to a stoppered cylinder, add 25 cc. of water, shake the mixture for one minute, filter through paper and divide into two portions; to one portion add 1 cc. of acetic acid and 0.5 cc. of water saturated with bromine: an immediate discoloration occurs; to the other portion add 0.1 cc. of tenth-normal potassium permanganate solution: a pale brownish-yellow color appears.

Transfer about 0.5 Gm. of evipal soluble to a 50 cc. Erlenmeyer flask, add 5 cc. of water and about 0.4 Gm. of *p*-nitrobenzyl chloride dissolved in 10 cc. of 90 per cent ethyl alcohol. Attach the flask to a reflux condenser and heat the mixture on a water bath for one-half hour. Cool the flask and collect the precipitate on a filter, wash with water, dry at 65 C., dissolve the dry product in 5 cc. of chloroform, filter, reprecipitate with alcohol and collect the precipitate; dry at 65 C.: the melting point of the product is 114-115 C.

Transfer about 0.3 Gm. of evipal soluble to a test tube containing 2 cc. of water and add, dropwise, a saturated solution of bromine in water until the color of bromine faintly persists after vigorously shaking the test tube. Pour the contents of the test tube into 100 cc. of water, filter through paper, wash with water and dry at 65 C.: the melting point of the product lies between 130 and 132 C., with decomposition.

Incinerate about 1 Gm. of evipal soluble in a porcelain dish, cool, dissolve the residue in 50 cc. of water and divide into two portions: the first portion responds to tests for sodium carbonate. Rinse the porcelain dish with 2 cc. of diluted hydrochloric acid, add the rinsings to the second portion and filter through paper: the filtrate yields no coloration or precipitation on saturation with hydrogen sulfide *(salts of heavy metals)*.

Boil about 0.5 Gm. of evipal soluble with 5 cc. of a 25 per cent sodium hydroxide solution: it is decomposed with evolution of ammonia.

Dissolve about 0.5 Gm. of evipal soluble in 10 cc. of water and divide the solution into two portions; to one portion add 1 cc. of mercuric chloride solution: a white precipitate results, insoluble in excess water, soluble in an excess of ammonia; to the other portion add 5 cc. of silver nitrate solution: a white precipitate results, soluble in excess water, soluble in an excess of ammonia.

Dissolve about 0.5 Gm. of evipal soluble in 50 cc. of water, add 5 cc. of diluted nitric acid, allow to stand for fifteen minutes and filter through paper: separate portions of 10 cc. each of the filtrate yield no opalescence on the addition of 1 cc. of silver nitrate solution *(chloride)*; no turbidity on the addition of 1 cc. of barium nitrate solution *(sulfate)*.

Add about 0.1 Gm. of evipal soluble to 2 cc. of sulfuric acid: the solution is pale yellow, gradually changing to brown-orange *(easily carbonizable substances)*.

Transfer about 1 Gm. of evipal soluble, accurately weighed, to a glass stoppered cylinder, add 50 cc. of anhydrous ether, stopper and shake for ten minutes; decant the supernatant liquid, filter through paper and repeat twice, using 25 cc., and 15 cc. portions of ether, respectively, utilizing the same filter; evaporate the combined filtrates to dryness in a tared beaker and dry to constant weight at 65 C.: the residue does not exceed 0.2 per cent *(uncombined cyclohexenyldimethyl barbituric acid)*. Dry about 1 Gm. of evipal soluble, accurately weighed, to constant weight at 65 C.: the loss in weight is negligible.

Transfer about 0.5 Gm., accurately weighed, of the dried evipal soluble to a tared porcelain dish, add 2 cc. of sulfuric acid, cautiously ignite until the excess of sulfuric acid has been volatilized, repeat the ignition twice with the addition of 1 cc. of sulfuric acid; add about 0.5 Gm. of ammonium carbonate; ignite to constant weight and weigh as sodium sulfate: the percentage of sodium corresponds to not less than 8.5 nor more than 9.4 when calculated to the dried substance.

Transfer about 0.5 Gm. of evipal soluble, accurately weighed, to a suitable separator, add 15 cc. of water, followed by the addition of 10 cc. of diluted hydrochloric acid; extract the mixture with eight successive portions of chloroform using 25 cc., 15 cc. and six portions of 10 cc., respectively, evaporate the combined chloroform extracts in a tared beaker to dryness in a stream of warm air and dry to constant weight at 65 C.: the amount of cyclohexenyl*di*methyl barbituric acid corresponds to not less than 91 per cent nor more than 92 per cent, calculated to the dried substance.

Dissolve the cyclohexenyl*di*methyl barbituric acid obtained as above, in 25 cc. of previously neutralized alcohol, add 25 cc. of recently boiled and cooled distilled water and titrate with tenth-normal sodium hydroxide solution, using thymolphthalein as an indicator: the amount of tenth-normal sodium hydroxide consumed corresponds to not less than 98.5 per cent nor more than 101.5 per cent of cyclohexenyl*di*methyl barbituric acid.

THEOPHYLLINE WITH ETHYLENEDIAMINE-U. S. P. (See New and Nonofficial Remedies, 1941, p. 583).

The following dosage forms have been accepted:

Tablets Aminophylline 0.0975 Gm. (1½ grains)
Prepared by E. S. Miller Laboratories, Inc., Los Angeles.
Tablets Aminophylline 0.195 Gm. (3 grains)
Prepared by E. S. Miller Laboratories, Inc., Los Angeles.
Ampul Solution Aminophylline, 2.4% W/V, 10 cc.
Prepared by E. S. Miller Laboratories, Inc., Los Angeles.
Ampul Solution Aminophylline 24% W/V in Ethylenediamine Solution 1% V/V (with Benzyl Alcohol 2% V/V), 2 cc.
Prepared by E. S. Miller Laboratories, Inc., Los Angeles.

PHENOLSULFONPHTHALEIN (See New and Nonofficial Remedies, 1941, p. 230).

The following dosage form has been accepted:

Ampuls Phenolsulfonphthalein Solution, 6 mg., 1 cc.
Each cubic centimeter of solution contains 6 mg. of phenolsulfonphthalein, in the form of the monosodium salt.
Prepared by Lakeside Laboratories, Inc., Milwaukee.

MERCURIC SUCCINIMIDE (See New and Nonofficial Remedies, 1941, p. 350).

Cheplin Biological Laboratories, Inc., Syracuse, N. Y.

Vial Solution Mercuric Succinimide, ⅙ grain (0.01 Gm.) in each cc., 30 cc.: Each cubic centimeter contains mercuric succinimide 0.01 Gm., benzyl alcohol 0.01 cc. and glycerin 0.013 Gm. in sufficient distilled water to make 1 cc.
Ampules Solution Mercuric Succinimide, ⅓ grain (0.02 Gm.), 1 cc.: Each 1 cc. ampule contains mercuric succinimide 0.02 Gm., benzyl alcohol 0.01 cc. and glycerin 0.013 Gm. in sufficient distilled water to make 1 cc.
Vial Solution Mercuric Succinimide, ⅓ grain (0.02 Gm.) in each cc., 30 cc.: Each cubic centimeter contains mercuric succinimide in sufficient distilled water to make 1 cc.

Flint, Eaton & Co., Decatur, Ill.

Ampul Solution Mercuric Succinimide, 0.01 Gm. (⅙ grain), 1 cc.

LIVER EXTRACT (INJECTABLE) U. S. P.-ENDO (See THE JOURNAL, March 29, 1941, page 1391, and Supplement to New and Nonofficial Remedies, 1941, page 12, under LIVER EXTRACT (INJECTABLE) U. S. P.-ENDO, 10 UNITS PER CC.).

The following dilution dosage forms have been accepted:

Liver Extract (Injectable) U. S. P.-Endo (5 U. S. P. units per cc.), 1 cc. Ampoule.
Liver Extract (Injectable) U. S. P.-Endo (2 U. S. P. units per cc.), 10 cc. vial.

THIAMINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1941, p. 551).

The following additional dosage forms have been accepted:

Tablets Thiamine Hydrochloride, 1 mg.; 5 mg.; 10 mg.
Prepared by Flint, Eaton & Co., Decatur, Ill.
Ampuls Solution Thiamine Hydrochloride, 10.0 mg., 1 cc.
Prepared by Flint, Eaton & Co., Decatur, Ill.
Vials Solution Thiamine Hydrochloride, 10 mg. per cc., 25 mg. per cc. and 50 mg. per cc. in 15 cc. vials.
Prepared by Flint, Eaton & Co., Decatur, Ill.
I. V. C. Thiamine Hydrochloride Crystalline Tablets, 5.0 mg. and 10 mg.
Prepared by the International Vitamin Corporation, New York. No U. S. Patent or trademark.

THIAMINE HYDROCHLORIDE-MERRELL (See New and Nonofficial Remedies, 1941, p. 553).

The following dosage forms have been accepted:

Thiamine Hydrochloride Tablets-Merrell, 5.0 mg. and 10.0 mg.

SODIUM THIOSULFATE (See New and Nonofficial Remedies, 1941, p. 503).

The following dosage forms have been accepted:

Ampuls Sodium Thiosulfate (Flint, Eaton & Co.), 0.5 Gm. (7½ grains), 5 cc.
Prepared by Flint, Eaton & Co., Decatur, Ill.
Ampuls Sodium Thiosulfate (Flint, Eaton & Co.), 1.0 Gm. (15½ grains), 10 cc.
Prepared by Flint, Eaton & Co., Decatur, Ill.

SULFATHIAZOLE (See New and Nonofficial Remedies, 1941, p. 519).

Sulfathiazole-Lakeside.—A brand of sulfathiazole-N. N. R.

Manufactured by Lakeside Laboratories, Inc., Milwaukee. No U. S. patent or trademark.
Tablets Sulfathiazole 0.5 Gm. (7.7 grains).

TETANUS ANTITOXIN BOVINE (See New and Nonofficial Remedies, 1941, p. 437).

The Gilliland Laboratories, Inc., Marietta, Pa.

Tetanus Antitoxin (Bovine), Gilliland.—A concentrated and refined antitoxin made from the blood serum of cattle hyperimmunized against the toxin of Clostridium tetani. Marketed in packages of one vial containing 1,500 units and in packages of one vial containing 10,000 units.

RINGER'S SOLUTION (See New and Nonofficial Remedies, 1941, p. 389).

Ringer's Solution in Vacoliter Container: Each hundred cubic centimeters contains sodium chloride U. S. P. 0.7 Gm., potassium chloride N. F. 0.03 Gm. and calcium chloride U. S. P. 0.025 Gm. Marketed in bottles (Vacoliter containers) of 500 cc. and 1,000 cc.
Prepared by Baxter Laboratories, Inc., Glenview, Ill., and Don Baxter, Inc., Glendale, Calif.

RIBOFLAVIN (See New and Nonofficial Remedies, 1941, p. 553).

Mead's Riboflavin Tablets, 1 mg.
Prepared by Mead Johnson and Company, Evansville, Ind.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JANUARY 10, 1942

ENROLMENT FOR SERVICE IN THE ARMY AND NAVY

Last week The Journal published an urgent request to all physicians of the United States to fill out the questionnaire published in that issue and mail it at once to Dr. Sam F. Seeley, Executive Officer of the Procurement and Assignment Service, Washington, D. C., indicating their availability to serve the nation in the present emergency. The response to this call to the medical profession to date has been highly gratifying. The following statement to that effect, with additional instructions, has been received from the Directing Board of the Procurement and Assignment Service:

The response of the physicians of the country to the Procurement and Assignment Service request for enrolment of those now ready for immediate service in the army or the navy is highly gratifying. All names are being processed, and those who meet the present demands of the Surgeon Generals will receive application forms and authority to appear for physical examination at an early date. All who are now ready for immediate duty should forward applications to the Procurement and Assignment Service at once. It is not the intention of the Procurement and Assignment Service to register every physician, dentist and veterinarian at the present time. Only those available for immediate assignments should register at this time. The physical requirements of all military, governmental, industrial and civil agencies will be published in national and state journals immediately. On the basis of this information every physician, dentist and veterinarian will be able to make a self appraisal of his physical qualifications. Within a few weeks the Procurement and Assignment Service will mail to all individuals a form on which they will be asked to state their preferences for assignment to all agencies of national defense which require medical, dental and veterinary personnel and for service in communities in public health and other civil categories. In this way every physician, dentist and veterinarian of the country will be able to lend maximum support to the national emergency. In order to meet the expanding needs of the military services, every physician immediately available for duty should mail his application blank to the Procurement and Assignment Service at once. All others will be given an opportunity to volunteer in the near future.

Frank H. Lahey, M.D., Chairman.
James E. Paullin, M.D.
Harvey B. Stone, M.D.
Harold S. Diehl, M.D.
C. Willard Camalier, D.D.S.
Sam F. Seeley, Major, M. C., U. S. Army, Executive Officer.

CALCIUM AND THE METABOLISM OF LEAD

Modern industry raises many questions in fields related to medicine. One of the problems of growing interest concerns the increased possibility of lead poisoning; paint pigments, tetraethyl lead in motor fuels, and spray materials used on fruits and vegetables are a few of many possible sources of exposure to lead under current ordinary living conditions. Numerous studies with a variety of analytic procedures have shown that practically all the body tissues contain measurable amounts of lead.

Of compelling interest is the similarity between the distribution and mobilization of lead and that of calcium and phosphorus. Experience with physicochemical models indicates that lead is transported in the blood as the secondary phosphate but is deposited in the bones as the insoluble tertiary phosphate.[1] Aub and his co-workers[2] have shown that not only is lead stored in the trabeculae of the long bones, as is the readily available calcium, but solution of parathyroid will mobilize this lead and the calcium in a parallel manner. Both roentgenographic evidence[3] and the results of intravenously administered radioactive lead[4] indicate its deposition and mobilization from those structures where shifts in calcium are likewise taking place. These and similar observations have led to the conception that lead and calcium are strikingly similar in their metabolism. In the toxic episode of lead poisoning it is advisable to immobilize the metal in the bones by promoting the concomitant deposition of calcium.[5] Subsequent treatment with acidifying agents such as ammonium chloride will bring forth the lead and the calcium into the blood stream, and deleading thus occurs.

With the organism in negative calcium balance such as occurs on a calcium-poor regimen, it might be expected that administered lead would be prevented from localizing in the bony trabeculae. However, a recent study by Shields and Mitchell[6] confirms earlier similar work that diets low in calcium or in phosphorus or in both promote increased lead retention. That this is due to circumstances within the gastrointestinal tract

1. Fairhall, L. T., and Shaw, C. P.: J. Indust. Hyg. **6:** 159 (Aug.) 1924. Fairhall, L. T.: J. Am. Chem. Soc. **46:** 1593 (Jan.) 1924.
2. Hunter, D., and Aub, J. C.: Quart. J. Med. **20:** 123 (Jan.) 1927.
3. Caffey, John: Radiology **17:** 957 (Nov.) 1931.
4. Behrens, B., and Baumann, A.: Ztschr. f. exper. Med. **92:** 251, 1933.
5. Aub, J. C.: The Biochemical Behavior of Lead in the Body, J. A. M. A. **104:** 87 (Jan. 12) 1935.
6. Shields, J. B., and Mitchell, H. H.: J. Nutrition **21:** 541 (June) 1941.

was shown by Lederer and Bing;[7] they found that the level of calcium in the ration exerts no influence whatever on the retention of lead when a lead salt is administered parenterally.

On the basis of current evidence, it appears that the mobilization of lead already deposited in the bones shows a striking parallel to the mobilization of calcium and that the absorption of lead from the intestine is influenced by the level of calcium in the diet. The deposition of lead in the bones appears to take place in inverse relation to that of calcium. Obviously, further study in this important field is necessary. From the point of view of public health, it is reassuring that an adequate intake of calcium and phosphorus presumably tends to protect the body against the assimilation of the small amounts of lead that are unavoidably taken into the gastrointestinal tract under ordinary conditions.

ISOIMMUNIZATION: ITS ROLE IN TRANSFUSION REACTIONS AND IN FETAL ERYTHROBLASTOSIS

For long it was believed that hemolytic transfusion reactions do not occur when patient and donor are alike with respect to the Landsteiner blood groups O, A, B and AB. In a recent paper, Wiener and Peters[1] pointed out that there are two classes of patients for whom this dictum does not hold. The first class includes patients who have been receiving repeated blood transfusions which have stimulated the appearance in the patient's serum of immune isoantibodies directed against the donor's cells, owing to blood factors unrelated to the four blood groups. For the second class of patients this explanation does not hold, as this class includes persons who have never previously undergone transfusion. All members of the second class, however, were found to be female patients ante partum or post partum. Wiener and Peters have suggested that these also represent cases of isoimmunization, the fetus in utero supplying the foreign antigen. This explanation had previously been proposed by Levine and Stetson[2] to explain a transfusion reaction in a case of pregnancy studied by them.

Of the blood properties which can give rise to isoimmunization, other than the factors A and B which determine the four Landsteiner blood groups, Wiener[3] has found the Rh factor most important. While isoimmunization as a result of repeated transfusion and in pregnancy is a relatively uncommon phenomenon, the Rh factor is the most apt to be responsible when it occurs. The Rh factor was first described by Landsteiner and Wiener[4] in 1940 and was so named because it was detected with an immune serum against rhesus blood. The factor is present in the blood of 85 per cent of persons in the normal population, regardless of the blood groups. As Wiener and Peters have shown, transfusions of Rh positive blood to Rh negative persons is well tolerated in the great majority of persons, but with occasional patients such transfusions give rise to isoimmunization. After the first transfusion in these cases the donor's blood is eliminated from the patient's circulation with few or no symptoms. Later, however, anti Rh isoantibodies appear in the patient's serum, so that subsequent transfusions of Rh positive blood may give rise to severe or even fatal reactions. Landsteiner and Wiener[5] have shown that the property Rh is inherited as a simple mendelian dominant. It is possible for an Rh negative mother to have an Rh positive child, namely, if the father is Rh positive. While such matings occur in about one seventh of all marriages, isoimmunization of the mother by the blood of the fetus is far less frequent. In certain rare instances, owing perhaps to some imperfection in the placenta, fetal blood escapes into the maternal circulation. As a result of such small repeated "transfusions" of Rh positive fetal blood, Rh negative mothers may produce anti Rh antibodies. Should the mother require a blood transfusion and the anti Rh isoantibodies not be detected in the cross match tests, a hemolytic reaction may result. A difficulty in the tests is that the agglutination reactions of many serums containing anti Rh isoagglutinins are not strong, but positive and negative reactions are more readily distinguished from the appearance of the sediment in the tests. Landsteiner and Wiener[5] describe an improved method for obtaining anti Rh immune serums by injecting guinea pigs with rhesus blood.

Shortly after the report by Wiener and Peters, Levine and Katzin[6] pointed out the close association between isoimmunization in pregnancy and pregnancy complications; Levine, Katzin and Burnham[7] suggested that this might be the cause of fetal erythroblastosis. If an Rh negative mother with an Rh positive fetus should produce anti Rh isoantibodies and these should filter back into the fetal circulation, they might have a destructive effect on the blood of the fetus and in this way give rise to symptoms of icterus gravis neonatorum or congenital hemolytic anemia. Subsequent studies in a larger series of cases have established the correctness of this theory beyond doubt. While only 15 per cent of persons in a random population are Rh negative, 90 per cent of mothers of erythro-

7. Lederer, L. G., and Bing, F. C.: Effect of Calcium and Phosphorus on Retention of Lead by Growing Organism, J. A. M. A. **114:** 2457 (June 22) 1940.

1. Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group, Ann. Int. Med. **13:** 2306 (June) 1940.

2. Levine, Philip, and Stetson, R. E.: An Unusual Case of Infra-Group Agglutination, J. A. M. A. **113:** 126 (July 8) 1939.

3. Wiener, A. S.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group: II. Further Observations on the Role of Property Rh, Particularly in Cases Without Demonstrable Isoantibodies, Arch. Path. **32:** 227 (Aug.) 1941.

4. Landsteiner, Karl, and Wiener, A. S.: An Agglutinable Factor in Human Blood Recognizable by Immune Sera for Rhesus Blood, Proc. Soc. Exper. Biol. & Med. **43:** 223 (Jan.) 1940.

5. Landsteiner, Karl, and Wiener, A. S.: Studies on an Agglutinogen (Rh) in Human Blood Reacting with Anti-Rhesus Sera and with Human Isoantibodies, J. Exper. Med. **74:** 309 (Oct.) 1941.

6. Levine, Philip, and Katzin, E. M.: Isoimmunization in Pregnancy and the Varieties of Isoagglutinins Observed, Proc. Soc. Exper. Biol. & Med. **45:** 343, 1940.

7. Levine, Philip; Katzin, E. M., and Burnham, Lyman: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Foetalis, J. A. M. A. **116:** 825 (March 1) 1941. Burnham, Lyman: The Common Etiology of Erythroblastosis Foetalis and Transfusion Accidents in Pregnancy, Am. J. Obst. & Gynec. **42:** 389 (Sept.) 1941.

blastotic infants have proved to be Rh negative.[8] Moreover, in many of the mothers' serums anti Rh agglutinins were detectable.

While the Rh factor has proved to be responsible for the great majority of instances of hemolytic reactions following transfusions of blood of the homologous group, a few instances have occurred in which this explanation did not hold. In these much less frequent cases other blood factors have been found to be at fault. Thus, Wiener[9] reports 2 instances of isoimmunization of A_2 patients against A_1 blood, 1 by repeated transfusion, the other as a result of pregnancy; Wiener and his collaborators have also observed the appearance of anti O isoagglutinins in the serum of a group AB patient given group O blood; and anti P agglutinins have been found in the serum of a P negative patient given P positive blood.[10] Similarly there are cases of fetal erythroblastosis in which the mother is Rh positive. Here it has been suggested that blood factors other than Rh may be responsible. For example, Levine and Polayes[11] have described an instance of isoinmunization in pregnancy in which the mother's serum contained an isohemolysin with reactions unrelated to Rh or any blood factor previously described. At times the situation may be complicated, as in a case recently reported by Wiener and Forer,[12] in which the serum of a group O person had two irregular agglutinins in it, one against the Rh factor, the other against agglutinogen M. For this patient only group O donors with blood of type N and lacking the Rh factor could be used. Two such donors were found among 90 group O donors tested, transfusions proving successful.

The observations of Wiener and his collaborators on intragroup hemolytic transfusion reactions and of Levine and his collaborators on fetal erythroblastosis are significant from the point of view of the individuality of human blood. With the factors A_1, A_2, B, M, N, P and Rh as many as seventy-two distinct types of human blood can be identified. With the additional factors that are identifiable with post-transfusion serums and serums from mothers of infants with fetal erythroblastosis, the number of subdivisions of human blood possible is further increased, as had also been shown with the aid of irregular isoagglutinin in normal human serums.[13] As examples one might mention the special hemolysin observed by Levine and Polayes[11] in a pregnancy serum and the observations of Wiener[3] that there are at least two sorts of Rh factor.

8. Levine, Philip; Vogel, P.; Katzin, E. M., and Burnham, L.: Pathogenesis of Erythroblastosis Foetalis: Statistical Evidence, Science **94:** 371 (Oct. 17) 1941.

9. Wiener, A. S.: Subdivisions of Group A and Group AB: II. Isoimmunization of A_2 Individuals Against A_1 Blood, with Special Reference to the Role of the Subgroups in Transfusion Reactions, J. Immunol. **41:** 181 (June) 1941.

10. Wiener, A. S.; Oremland, B. H.; Hyman, M. A., and Samwick, A. A.: Transfusion Reactions: Experiences with More Than 3,000 Blood Transfusions, Am. J. Clin. Path. **11:** 102 (Feb.) 1941.

11. Levine, Philip, and Polayes, S. H.: An Atypical Hemolysin in Pregnancy, Ann. Int. Med. **14:** 1903 (April) 1940.

12. Wiener, A. S., and Forer, S.: A Human Serum Containing Four Distinct Isoagglutinins, Proc. Soc. Exper. Biol. & Med. **47:** 215 (June) 1941.

13. Landsteiner, Karl, and Levine, Philip: Isoagglutinin Reactions of Human Blood Other Than Those Defining Blood Groups, J. Immunol. **17:** 1 (July) 1929.

Current Comment

1942 DUES NOW PAYABLE

For the convenience of Fellows and subscribers who have not paid the 1942 dues, a colored reminder slip is enclosed in this issue of THE JOURNAL. It takes the place of a personal statement, and its use by those who have not yet paid for 1942 will result in a tremendous saving of postage and clerical work in the Headquarters office. The slip is cut so that when folded it forms a ready addressed, ready stamped envelop for check, money order or draft. It lists not only THE JOURNAL but all the special journals of the Association, with their respective subscription prices—likewise *Hygeia,* the Health Magazine. Thus payment for all publications desired may be covered with one remittance. If you have already paid for 1942, please disregard the slip.

BEHAVIOR OF GLYCERIN IN THE ANIMAL ORGANISM

Glycerin is widely employed in pharmaceutic preparations, perhaps more frequently than any other substance except water. Any toxic properties which it may possess, therefore, are important. Deichmann[1] concludes that glycerin is absorbed from the peritoneum, the gastrointestinal tract and subcutaneous tissue but that its penetration of the intact skin appears to be negligible. Toxic doses of glycerin produce characteristic signs and symptoms and in sufficient quantities can cause death. Intravenous injection of even small doses results in a transient fall in the arterial blood pressure and an increased rate and magnitude of respiration. A lethal oral dose will produce a slowly failing circulation, while a lethal intraperitoneal injection produces a stimulation of respiration and finally a sudden drop of arterial blood pressure. Death is due to the combined effects of failing circulation and respiration. Diuresis appears to be more pronounced after oral than after subcutaneous administration. A portion of absorbed glycerin is transformed in the organism into dextrose and subsequently into glycogen. Glycerin appears to exert a protein-sparing action if administered in concentrations well below the toxic level. The pathologic changes reported in cases of experimental glycerin poisoning are those of acute toxic damage to the liver, kidneys and lungs. The gastrointestinal tract may suffer after the administration of large oral doses, and the subcutaneous tissue may develop pronounced local damage at the site of injection. Although the toxic effects of glycerin as summarized are impressive, it must be pointed out, as Deichmann did, that there are only two cases on record in which glycerin has been known to produce poisoning; these were in children. The toxic effects of this substance, therefore, must be considered as clinically important only in the event of gross overdosage or in the presence of hypersensitivity.

1. Deichmann, Wilhelm: Glycerol: Behavior in the Animal Organism (A Review of the Literature), Indust. Med., October 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

INFLUENZA

Circular Letter No. 124

The following statement summarizing our present concepts of influenza has been prepared for the Surgeon General by the director of the Commission on Influenza of the Board for the Investigation and Control of Influenza and other Epidemic Diseases in the Army:

1. *Definition.*—Influenza is an acute respiratory disease of virus origin which occurs almost annually in epidemics of varying severity. Two distinct types (types A and B) of virus have been identified; others are suspected. The diagnosis should not be limited to outbreaks of high mortality, such as that of the autumn of 1918. The presence of influenza should be suspected when an undue incidence of unidentified, febrile, upper respiratory disease is encountered.

2. *General Features.*—The usual epidemic is characterized by its sudden appearance in a cantonment, its rapid spread to a peak in from three to four weeks, attacking from 10 to 40 per cent of the population, its low mortality, and its prompt subsidence in from six to eight weeks after onset.

In the average patient the onset is sudden, with chills or chilliness, pharyngeal irritation, generalized aches, prostration and slight dry cough. Respiratory symptoms are not prominent. The temperature reaches 100-103 F., and leukopenia or absence of leukocytosis is the rule. The febrile course lasts from three to five days, followed by relatively prompt recovery except for residual fatigue. An exaggeration of fever or an increase in severity of symptoms indicates the probability of respiratory complications, which vary from tracheitis and bronchitis to extensive pneumonia and empyema.

Complications are usually due to secondary bacterial invaders. The mortality varies with the nature and virulence of the bacterial agents. There may be rapidly fatal cases in which the virus infection is accompanied from the onset by bacterial infection; but more commonly the bacterial complications develop about the time of convalescence from the primary disease.

The virus can be recovered in experimental animals and from the nose and throat secretions of infected individuals. Tests with the patient's serum may be used to identify the disease by demonstrating a rise in antibodies specific for the type of virus present. Immunity develops in convalescence and is effective for an indefinite period, probably longer than is usually assumed.

Approximately one fourth of a population may undergo subclinical infection and during the epidemic period serve as important agents in the transmission of infection.

3. *Control.*—(*a*) General Measures: General control measures should be directed not only toward the prevention of the transmission of influenza virus but also toward the protection of incipient cases and early convalescents from secondary infection with pathogenic bacteria. The virus of influenza is transmitted through the upper respiratory tract by direct droplet infection from an infected individual or by indirect infection with discharges from his respiratory tract. Crowding is a most important factor in the spread of the disease. In the presence of an epidemic, unnecessary congregation in mess halls, recreation centers or barracks should be eliminated, and existing regulations concerning ventilation and bed space in barracks and hospitals should be carried out. If the epidemic is severe, working quarantine of small units may be desirable.

New or unseasoned troops should be segregated, and the transfer of troops to and from infected camps should be discouraged. The transfer by train or transport of bodies of troops infected with influenza is particularly hazardous. Their close association under such conditions will result in the infection of many who would otherwise escape and in a high incidence of complications and deaths which otherwise would be avoided.

The control measures prescribed in paragraphs 2, 3 and 10, AR 40-220, should be strictly enforced. The admission and general management in hospital is clearly outlined in AR 40-245.

(*b*) Specific Measures: At present no specific control measure has been established, although vaccination methods are under investigation.

4. *Treatment.*—The treatment in uncomplicated cases of influenza is at present symptomatic. There is no evidence that chemotherapy influences the primary virus disease. The patient should be kept warm in bed for forty-eight hours after his temperature has returned to normal. Cold air frequently aggravates the irritation of the respiratory passages. Steam inhalations and soothing cough mixtures with codeine often relieve a persistent distressing cough. Mild antipyretics and sedatives may be used, but narcotics other than codeine are generally contraindicated. Fluids should be given to 3,000 cc. or more daily. The bowels should be regulated when necessary with mild cathartics or enemas. A soft diet can be given as soon as the patient's appetite will tolerate it.

The patient should resume his normal activities gradually. When secondary bacterial invaders are prevalent, protective isolation for a week or more after recovery should be given. Any unexplained rise of temperature or a return of fever should be interpreted as the onset of pulmonary disease due to pathogenic bacteria. Under these conditions adequate measures for the diagnosis of pneumonia and the determination of the infecting bacterial agent should be instituted. Chemotherapy or other available types of therapy directed against the invading bacterium should be used.

By order of the Surgeon General:

JOHN A. ROGERS,
Lieutenant Colonel, Medical Corps,
Executive Officer.

FIRST AID INSTRUCTORS—RED CROSS APPEALS FOR FUNDS

The American Red Cross has sent to San Francisco twenty experienced first aid field representatives who were dispersed at once to strategic points and set to work training lay instructors in first aid throughout the Pacific Coast states.

The lay instructor's course covers forty-five hours of class work and practical application of first aid. For those who already hold Red Cross standard and advanced first aid certificates, this period is reduced to fifteen hours. Those who qualify as instructors are authorized to teach both standard and advanced courses in emergency care of the injured. Red Cross first aid certificates will be awarded to those who successfully complete the latter courses. Doctors who are graduates of recognized medical schools may receive an instructor's appointment from the Red Cross on application to National Headquarters in Washington, D. C., or to the area headquarters in San Francisco, St. Louis and Alexandria, Va.

The Red Cross now has more than thirty-five thousand first aid instructors throughout the country who are busy meeting the demands for training in their local communities. During the past year upward of a million persons received first aid training from Red Cross instructors. Of these about one hundred thousand were residents of California, Oregon, Washington, Idaho, Utah, Arizona and Nevada.

First aid instruction is one of the Red Cross activities on behalf of civilian defense. During the past year local chapters have been organizing and training volunteer first aid detachments to be ready for immediate service in industrial establishments and residential areas in case of explosion, fire, sabotage or other incidents requiring the services of first aiders. Every effort is being made to protect defense industries by means of these first aid detachments. First aid instruction is also being furnished by the Red Cross to soldiers and sailors. This work, which embraces every conceivable type of morale building activity, among the men in uniform as well as their families, has been greatly expanded during the past year.

Because of the heavy financial burden occasioned by its war activities, the Red Cross has appealed for a special fund of $50,000,000.

RESERVE COMMISSIONS FOR MEDICAL STUDENTS

The National Headquarters of the Selective Service System stated January 1 that Brig. Gen. Lewis B. Hershey, director of Selective Service, has advised all local boards through their state headquarters that third and fourth year students in acceptable medical schools and first year interns may obtain reserve commissions in the Army or Navy and then will be permitted to complete their medical training, including one year of internship, before being ordered to active duty. Such medical students and interns may be deferred by their local boards in class II-A pending receipt of their commissions, but all who are eligible for a commission and do not apply may be considered for classification in class I-A if they are not deferred for other reasons and are found physically qualified for general military service.

Third and fourth year medical students and interns who are rejected after applying for commissions, and also first and second year medical students and those registrants who have been accepted as students in a medical school, may be deferred in class II-A as long as their school officials certify that they give indication that they will become qualified medical practitioners, General Hershey said. He emphasized, however, that no group deferment is permissible under the law and that each case must be decided by a local board on the facts concerning the individual registrant involved.

Medical students and interns accepted by the Army are given commissions as second lieutenants pending graduation when they become first lieutenants in the Army Medical Reserve Corps. Those accepted by the Navy are commissioned as ensigns until graduation, when they become lieutenants (junior grade) in the Navy Medical Reserve Corps.

BRITISH AMERICAN AMBULANCE CORPS

Since the entrance of the United States into the war and after consultation with representatives of the allied governments, the British American Ambulance Corps has decided to concentrate its efforts in the future on supplying ambulances and a limited number of mobile canteens, leaving to other relief organizations the sending of other essential medical supplies. However, contributions will be accepted for stretchers, blankets and first aid cases to the extent that they are needed to equip ambulances. The British American Ambulance Corps will continue with no diminution of effort to raise funds for ambulances for the allied cause and will bend every effort to raise not only the number now needed but a sufficient number to use as a reserve to meet without delay any emergency that may arise. Ambulances will not be accepted, therefore, for any particular country or front. Only one particular type of ambulance will be purchased, and it is so constructed that it can do service in both tropical and cold climates. The sides and top are demountable and may be packed flat in the chassis in order to reduce space required for shipping. This standardized type of ambulance is sturdy, will attain a speed of 60 miles an hour on good roads and will stand up under desert or other rough conditions. These ambulances cost $2,000 each.

Recently the British American Ambulance Corps has had demand from several cities in the United States for ambulances and a few weeks ago had a request from London for two hundred and fifty-six ambulances to serve with the Royal Air Force as a result of the great expansion recently in the Royal Air Force in airplanes and personnel and not proportionately in its ambulance service. Ambulances are not included under the terms of the lend-lease bill. The ambulances donated by groups, corporations or clubs may be marked with any inscription the donor desires, but a promise cannot be made that they will be sent to any particular location.

PERCENTAGE OF CALIFORNIA REGISTRANTS REJECTED

The final figures showing the results obtained by the California boards and their physicians under the old plan of "primary selective service medical examination and classification" before presenting registrants to army examiners at induction stations, are as follows:

Of 60,839 selectees presented to induction stations 5,430 were rejected there (8.92 per cent).

Rejections for physical and mental reasons (excluding illiterates)	8.33%
Rejections for reasons other than physical or mental (includes illiterates)	0.59%
Percentage of rejections for the state	8.92%

Breakdown of the 8.92 per cent rejected:

	Per Cent
Eyes (vision principally)	11.5
Teeth (number, pyorrhea, malocclusion)	9.5
Weight (mostly underweight, very few overweight)	4.0
Ear (chronic catarrhal otitis media, membrane)	7.5
Cardio-vascular (heart, blood pressure, pulse)	3.5
Spine joints	3.0
Genito-urinary (venereal, gonorrhea, syphilis, testicle)	5.0
Abdominal organs (hernia, gallbladder, appendix, rectum)	5.5
Nose, mouth (larynx, septum)	2.5
Neuropsychiatric	16.5
Extremities (digits, muscles, pes planus, varicose veins, fractures)	14.0
Lungs	9.5
Endocrine (and skin)	2.0
Other than physical (illiteracy, felonies, dishonorable discharge, inaptitude)	6.0
	100

ARMY HOSPITAL NAMED FOR GENERAL DARNALL

The hospital leased by the War Department from the commonwealth of Kentucky at Danville has been designated as "Darnall General Hospital" in honor of the late Brig. Gen. Carl Rogers Darnall, who died in Washington, D. C., Jan. 18, 1941. General Darnall was born in Texas on Dec. 25, 1867 and graduated from Jefferson Medical College in 1890. He entered the military service on Oct. 27, 1896 and his first service was at Fort Clark, Texas, as medical officer with the Twenty-Third Infantry. Later he commanded the military hospital at Iloilo, Philippine Islands. He then served from 1903 to 1913 as secretary of the faculty and instructor at the Army Medical School, Washington, D. C. During the first World War he served as executive officer in the Surgeon General's Office. In 1929 he was appointed Assistant Surgeon General with the rank of brigadier general and was serving in this capacity at the time of his retirement in 1931. General Darnall was awarded the Distinguished Service Medal for organizing and administering the Supply Division of the Medical Department during the World War. He was credited with originating the use of liquid chlorination of water when he was at the Army Medical School as professor of chemistry.

MEDICAL DEFENSE MEASURES IN THE CHICAGO AREA

At a meeting of the defense medical advisory council appointed by the mayor of Chicago, the president of the Chicago Board of Health, Dr. Herman N. Bundesen, announced the creation of a 100 mile emergency medical zone for Chicago and vicinity, including Cook, DuPage and Lake counties in Illinois and part of Lake County in Indiana. The defense medical advisory council will coordinate in this area all hospitals, dispensaries, first aid stations and training stations. The major defense of the medical defense plan called for the organization of two field units for each hospital, organization of emergency

ambulance service, the conversion of trucks into ambulances, the creation of a blood reserve, a campaign for typhoid vaccination and the inventory of all hospitals in this area, with a tabulation of the bed capacity, x-ray equipment, respirators, operating rooms and laboratories.

Chicago's first free ambulance service and mobile operating room equipped for catastrophes and emergencies went into operation on December 17 as a unit of Chicago's only all Negro hospital, Provident Hospital. This service is sponsored by the hospital as a defense measure. There will be two ambulances in this service, one with facilities for transporting 5 patients and equipped to care for 100 patients at the scene of accidents. Its special equipment includes not only four doctors, four nurses and equipment for performing operations in the field but also portable fire fighting apparatus, wrecking tools and an acetylene torch.

The officers of the various women's clubs presented to Mayor Kelly on December 16 the names of thirty-five thousand women who offered their services for defense work, and the work of classifying these women for the various chores was begun at once.

ANNUAL MEDICOMILITARY SYMPOSIUM ON NUTRITION

The annual medicomilitary symposium in the second military area will be held on Tuesday, January 13, at 8:30 p. m. in room 1316X at 90 Church Street, New York City, the general theme of the evening being nutrition in the army. Physicians, dentists, veterinarians, nurses, dietitians, students of professional schools and nutrition experts are cordially invited, as are representatives of the American Red Cross. Lieut. Col. James A. Tobey, Sanitary Corps, will discuss "Nutritional Problems in the Army," Major Louis Griessman of the veterinary reserve "Inspection of Foods in the Army," Col. Samuel A. Cohen of the Medical Corps "The Army Medical Officer and Nutrition," Col. Hyman I. Teperson of the Medical Corps "The Roentgen Ray in the Diagnosis of Nutritional Disorders" and Col. John L. Kantor of the medical corps will give a general summary. Lieut. Col. J. K. Surls of the medical corps will preside. Col. Milton I. Strahl of the medical reserve is chairman of the executive committee. There will be exhibits on army nutrition. The banquet which had been planned for this meeting has been canceled because of the emergency.

OFFICERS, SAILORS AND EMPLOYEES DONATE AMBULANCES

On Dec. 10, 1941 a cavalcade of twelve ambulances, Norfolk's newest gift to the British American Ambulance Corps, left for the United States Naval Base at Norfolk, Va., where they were officially presented to William V. C. Ruxton on the following Friday. The $24,000 necessary to purchase these ambulances came as a donation from the officers, enlisted personnel and civilian employees of the Norfolk Navy Yard. The campaign was conducted under the direction of Mr. Herbert J. Gerst, British American Ambulance Corps chairman for Norfolk, with the cooperation of Admiral Manley H. Simons of the Navy Yard. In addition to the twelve ambulances the British American Ambulance Corps will receive an additional $2,000 for an ambulance previously donated by the citizens of Norfolk in memory of Lieut. Comdr. Heywood L. Edwards, who went down with the U. S. Destroyer *Reuben James*.

THE ARMY MEDICAL DEPARTMENT

The history of the Medical Department of the U. S. Army commences with the siege of Boston in 1775. The Second Provincial Congress of Massachusetts Bay provided for examination of persons seeking appointment as surgeons in the colonial forces. Two surgeons and two surgeon's mates were allowed to a hospital, and one surgeon and two mates for a regiment in the field. No method for the evacuation of battlefield casualties existed, and none was perfected until the Civil War, when a surgeon of the Union forces, Jonathan Letterman, devised a system that has become the basic pattern of the field medical service of all the great powers.

In the first issue of Army Regulations, in 1779, the provisions governing medical service consisted of little more than an injunction to provide sick and wounded soldiers with fresh straw on which to lie, and prescribed, in event of death, the procedure to be followed.

The vast army medical organization of today is equipped and trained for field service with hospitals costing $160,000,000 and with a budget of $85,000,000 for the current year. However great the changes since the Revolutionary War, the mission of the Medical Department endures unaltered. Army Regulations describe this mission as "conservation of man power." The accomplishment devolves on three factors: (1) selection and enrolment of those physically fit for military duty, (2) maintenance of health of military personnel by application of preventive medicine and (3) furnishing to the disabled such aid in the form of evacuation and hospitalization as will speedily restore them to health and fighting efficiency.

REFRESHER COURSES FOR NURSES

Graduate nurses in the Detroit area who have not recently been active may review their professional skills in a course to be given by Wayne University at St. Mary's and Evangelical Deaconess Hospitals, Detroit, beginning January 12. One hundred and sixty-one persons have already taken advantage of five similar courses, already completed. There are no fees, as funds have been made available by the State Board of Control for Vocational Education and the W. K. Kellogg Foundation. Applicants must be graduate nurses living in Michigan. Registrations are now being taken by Mrs. Lulu St. Clair Blaine, director of the Community Nursing Bureau and registrar for the course, at 51 West Warren, Detroit.

BRITISH WAR RELIEF ASSOCIATION OF NORTHERN CALIFORNIA

The British War Relief Association of Northern California reports that at the end of another year only one shipment among large quantities of medical and surgical supplies that have been shipped to the British Red Cross has failed to reach its destination. Through the cooperation of the San Francisco County Medical Association, dried blood plasma has been sent to the British commands in Singapore and Hongkong, and portable transfusion kits were placed on board H. M. S. *Liverpool* and *Orion*. As an example of the interest in British war relief in northern California, Dr. John R. Upton sites the Hanford Union High School, whose gift largely made it possible to place the transfusion kits aboard the *Orion*.

SYMPOSIUM ON MILITARY MEDICINE

The Long Island College of Medicine, Brooklyn, sponsored a symposium on military medicine, December 3. The speakers were:

Rear Admiral Charles M. Oman, M. C., U. S. Navy, commanding officer, U. S. Naval Medical Center, Washington, D. C., Medical Tactics as Applied to Naval Warfare.

Capt. Paul M. Albright, M. C., U. S. Navy, Washington, D. C., Eyes of the Navy (illustrated with sound film).

Dr. Philip D. Wilson, New York, Fractures in Modern War.

Capt. Dickinson S. Pepper, M. R. C., U. S. Army, Washington, D. C., The Medical Student and the Military Service.

Comdr. Page O. Northington, flight surgeon, U. S. Navy, New York, Aviation Medicine.

OFFICE OF SURGEON GENERAL MOVED

The office of the Surgeon General of the United States Army in Washington, D. C., has been moved from the new Social Security Building, Fourth and C streets S.W., to 1818 H Street N.W.

ORGANIZATION SECTION

OFFICIAL NOTES

FOURTH ANNUAL CONGRESS ON INDUSTRIAL HEALTH

Sponsored by the Council on Industrial Health of the American Medical Association, January 12-14, at the Palmer House, Chicago: Stanley J. Seeger, M.D., Chairman, Texarkana, Texas; Harvey Bartle, M.D., Philadelphia; Leverett D. Bristol, M.D., New York City; Warren F. Draper, M.D., Washington; Philip Drinker, Boston; Leroy U. Gardner, M.D., Saranac Lake, N. Y.; Raymond Hussey, M.D., Baltimore; Henry H. Kessler, M.D., Newark; Anthony J. Lanza, M.D., New York City; Robert T. Legge, M.D., Berkeley, Calif.; C. W. Roberts, M.D., Atlanta; Clarence D. Selby, M.D., Detroit, and C. M. Peterson, M.D., Secretary, Chicago.

MONDAY MORNING, 9:00

REGISTRATION. NO FEE. *RED LACQUER ROOM*

MONDAY MORNING, 9:45

STANLEY J. SEEGER, M.D., PRESIDING

Report of the Council on Industrial Health.
STANLEY J. SEEGER, M.D., Texarkana, Texas.

Medical Aspects of Vocational and Industrial Training.
W. A. SAWYER, M.D., Rochester, N. Y.
Chairman, Committee on Industrial Health, Section on Preventive and Industrial Medicine and Public Health, American Medical Association.

The Physiology of Work.
A. C. IVY, M.D., Chicago.
Professor of Physiology, Northwestern University School of Medicine.

LECTURE ON INDUSTRIAL MEDICINE
TUBERCULOSIS IN INDUSTRY—A RÉSUMÉ

LEROY U. GARDNER, M.D., Saranac Lake, New York.
Director, The Saranac Laboratory for the Study of Tuberculosis.

Procurement and Assignment of Physicians for Industry.
SAM F. SEELEY, M.D., Washington, D. C.
Executive Officer, Procurement and Assignment Service, Office of Defense Health and Welfare Services.

RED LACQUER ROOM

MONDAY AFTERNOON, 2:30

WARREN F. DRAPER, M.D., PRESIDING

A Dental Program for Industry.
R. M. WALLS, D.D.S., Bethlehem, Pa.
Chairman, Committee on Economics, American Dental Association.

Industrial Dermatoses.
A Report by the Committee on Industrial Dermatology, Section on Dermatology and Syphilology, American Medical Association.
C. GUY LANE, M.D., Chairman
CHARLES C. DENNIE, M.D.
JOHN G. DOWNING, M.D.
HARRY FOERSTER, M.D.
EDWARD A. OLIVER, M.D.
MARION SULZBERGER, M.D.

The Panel System in Workmen's Compensation Administration.
DAVID J. KALISKI, M.D., New York City.
Director, Committee on Workmen's Compensation, Medical Society of the State of New York.

Mass Roentgenography of the Chest for the United States Army.
MAJOR ALFRED A. DE LORIMIER, M.C., Washington, D. C.
Director, Department of Roentgenology, Army Medical School.

RED LACQUER ROOM

MONDAY AFTERNOON, 2:30

LEVERETT D. BRISTOL, M.D., PRESIDING

SYMPOSIUM ON UNDERGRADUATE INDUSTRIAL MEDICAL EDUCATION

Present Problems in Curriculum Adjustment.
RAYMOND B. ALLEN, M.D., Chicago.
Executive Dean, Chicago Colleges, University of Illinois.

Industrial Health—A Separate Discipline.
T. LYLE HAZLETT, M.D., East Pittsburgh, Pa.
Professor of Industrial Hygiene, University of Pittsburgh School of Medicine.

Correlation of Industrial Hygiene Instruction with Other Clinical Training.
DONALD E. CUMMINGS, Denver.
Director, Division of Industrial Hygiene, University of Colorado School of Medicine and Hospitals.

The Industrial Clinical Clerkship.
FRED J. WAMPLER, M.D., Richmond.
Professor of Preventive Medicine, Medical College of Virginia.

Industrial Experience in the Internship.
WILL F. LYON, M.D., Chicago.
Assistant Professor of Surgery, University of Illinois College of Medicine.

The Occupational Disease Clinic.
MILTON H. KRONENBERG, M.D., Chicago.
Assistant Professor of Bacteriology and Public Health, University of Illinois College of Medicine.

ROOM 17

MONDAY EVENING, 6:30

STATE SOCIETIES DINNER AND ROUND TABLE
ANTHONY J. LANZA, M.D., PRESIDING

An informal dinner and round table discussion, intended primarily for committees on industrial health in state and county medical societies, will be held. Topics and discussion leaders will be:

Professional Relations.
ANTHONY J. LANZA, M.D., New York City.
Chairman, Committee on Professional Relationships, Council on Industrial Health, American Medical Association.

Industrial Health and the War.
CLARENCE D. SELBY, M.D., Detroit.
Chairman, Subcommittee on Industrial Health and Medicine, Health and Medical Committee, Federal Security Agency.

Visiting Nurses in Industry.
MISS JOANNA JOHNSON, R.N., Milwaukee.
Chairman, Industrial Nursing Section, National Organization for Public Health Nursing.

Progress in Official Agencies.
J. J. BLOOMFIELD, Bethesda, Md.
Chief, States' Relations Section, U. S. Public Health Service, National Institute of Health.

Postgraduate Education in Industrial Health.
WALTER L. BIERRING, M.D., Des Moines.
Commissioner, State of Iowa Department of Health.

CRYSTAL ROOM

TUESDAY MORNING, 9:30

HENRY H. KESSLER, M.D., PRESIDING

Conservation of Manpower in Connecticut.
CLIFFORD KUH, M.D., New Haven.
Chairman, Committee on Industrial Health, Connecticut State Medical Society.

Health Education for Industrial Workers.
LEVERETT D. BRISTOL, M.D., New York City.
Chairman, Committee on Education and Publications, Council on Industrial Health, American Medical Association.

LECTURE ON TRAUMATIC SURGERY
WOUND HEALING

EDWARD L. HOWES, M.D., New York City.
Associate Professor of Surgery, Columbia University College of Physicians and Surgeons.

The Field of Industrial Ophthalmology.
A Report by the Committee on Industrial Ophthalmology, Section on Ophthalmology, American Medical Association.
ALBERT C. SNELL, M.D., Chairman.
ARTHUR CULLER, M.D.
HEDWIG S. KUHN, M.D.

Placement of the Worker in Industry.
JOSEPH TIFFIN, PH.D., Lafayette, Ind.
Professor of Industrial Psychology, Purdue University.

RED LACQUER ROOM

TUESDAY AFTERNOON, 2:30

ROBERT T. LEGGE, M.D., PRESIDING

Conservation of Hearing in Industry.
C. C. BUNCH, PH.D., Evanston, Ill.
Department of Speech Reeducation, School of Speech of Northwestern University.

Recent Trends in Physical Examinations Under Civil Service.
VERNE K. HARVEY, M.D., Washington, D. C.
Medical Director, U. S. Civil Service Commission.

Vitamin Administration in Industry.
A Report Prepared by Representatives of the Council on Foods and Nutrition and the Council on Industrial Health.
J. S. McLESTER, M.D.
GEORGE R. COWGILL, PH.D.
R. M. WILDER, M.D.
LEVERETT D. BRISTOL, M.D.
LEROY U. GARDNER, M.D.
CLARENCE D. SELBY, M.D.

Medical Service Plans for Small Industry.
MYER S. BLOOM, M.D., Binghamton, N. Y.

RED LACQUER ROOM

WEDNESDAY, JANUARY 14

CLINICAL PROGRAM

University of Illinois College of Medicine
1853 West Polk Street, Room 423
Chicago

DAVID JOHN DAVIS, M.D., PRESIDING

9:30 A. M.

Pulmonary Capacity Tests in Health and Disease. Demonstration.
GEORGE E. WAKERLIN, M.D., Professor of Physiology.

Difficulties and Fallacies of Interpretation of Chest X-Ray Films. Demonstration.
ADOLPH HARTUNG, M.D., Professor of Radiology.

Practical Points on Patch Testing in Occupational Dermatitis. Demonstration.
LEONARD F. WEBER, M.D., Associate Professor of Dermatology.

Urinary, Blood and Other Tests of Value in Cases of Industrial Toxicology. Demonstration.
WILLIAM D. McNALLY, M.D., Coroner's Chemist, Cook County, Chicago.

2:00 P. M.

MILTON H. KRONENBERG, M.D., PRESIDING

Evaluating the Traumatic Abdomen.
CHARLES A. PUESTOW, M.D.
Associate Professor of Surgery.

Dental and Oral Manifestations of Occupational Origin.
ISAAC SCHOUR, D.D.S., Ph.D., Professor of Dental Histology, and BERNARD SARNAT, D.D.S., M.D., College of Dentistry.

The Industrial Hernia—Is It a Cause for Rejection?
WILL F. LYON, M.D.
Associate Professor of Surgery.

The Occupational Anemias.
CARROLL BIRCH, M.D.
Assistant Professor of Medicine.

Special Events

WEDNESDAY, JANUARY 14

Field trips have been arranged for a limited number of physicians registered at the Fourth Annual Congress on Industrial Health who are interested in details of industrial medical department administration. These field trips are available only to citizens of the United States. Those who wish to take the trips should apply for cards at the Registration Desk of the Congress on Monday or Tuesday, January 12-13.

WESTERN ELECTRIC COMPANY
HAWTHORNE WORKS

Cicero Ave. and 24th Street, Chicago

10 a. m. INSPECTION OF PREEMPLOYMENT PHYSICAL EXAMINATIONS UNIT AND MAIN HOSPITAL.
1 p. m. LUNCHEON IN MAIN RESTAURANT.
1:30 p. m. DISCUSSION OF THE WORK OF THE PERSONNEL COUNSELING DIVISION.
(Bus transportation will leave Palmer House, Wabash Avenue Entrance, about 9 o'clock Wednesday morning.)

CARNEGIE-ILLINOIS STEEL CORPORATION
GARY, INDIANA

Clinics and Demonstration in Surgical Department

10:30 a. m. VISIT TO GARY WORKS EMERGENCY HOSPITAL.
(Surgical Rooms, Dental Department, Physical Therapy Department, X-Ray Department, Preemployment Physical Examinations Department.)
11:30 a. m. TOUR OF GARY WORKS.
Mr. S. M. Jenks, General Superintendent of Gary Works.
12:30 p. m. LUNCHEON IN LUNCH CLUB.
Mr. S. M. Jenks, Toastmaster.
1:30 p. m.
DISCUSSION OF SAFETY METHODS, INCLUDING RESUSCITATION METHODS.
Mr. Earl Fyler.
J. C. Donchess, M.D.
TREATMENT OF FRESH WOUNDS.
J. C. Donchess, M.D.
VALUE OF DENTAL HYGIENE.
H. R. Klieber, D.D.S.
TREATMENT OF BURNS—COLORED MOVING PICTURE.
C. R. Zeiss, M.D.
PREVENTION AND TREATMENT OF HEAT SICKNESS—COLORED SOUND PICTURE.
RICHARD J. BENNETT JR., M.D.
DEMONSTRATION OF SPLINTS AND APPLIANCES.
F. M. Merritt, M.D.
FRACTURE MANAGEMENT, INCLUDING COMPOUND FRACTURES.
Philip H. Kreuscher, M.D., and Staff.
(Transportation will be provided, leaving the Palmer House, Wabash Avenue entrance, at 9 o'clock Wednesday morning.)

THE ATLANTIC CITY SESSION

Applications for Space in the Scientific Exhibit

Applications for space in the Scientific Exhibit at the Atlantic City session, both for exhibits and for motion pictures, close on January 20. Application blanks may be obtained from the section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

FEDERAL INCOME TAX ON ACCOUNTS RECEIVABLE

PREPARED BY THE BUREAU OF LEGAL MEDICINE AND LEGISLATION

Prior to 1934, if a taxpayer died who had been on a cash receipts and disbursements basis for federal income tax purposes, the collectible accounts outstanding on his books at the time of death were not subject to income tax, and most physicians use this method in reporting their incomes for federal taxation. Income tax was not paid on such accounts by any one, even though each account was collected in full after the taxpayer's death. The Congress in 1934 acted to close this gap in the income tax structure by passing an amendment to the income tax act which now appears as a part of section 42 of the Internal Revenue Code:

> In the case of the death of a taxpayer there shall be included in computing net income for the taxable period in which falls the date of his death, amounts accrued up to the date of his death if not otherwise properly includible in respect of such period or a prior period.

Under this amendment, if a federal income taxpayer dies during the tax year, who has customarily executed his return on a cash receipts and disbursements basis, the return for the tax year of death must include as income not only the cash receipts but also a fair value of the outstanding accounts on the books of the taxpayer at the time of his death. At the same time that the Congress enacted this amendment it also amended section 43 relating to the period for which deductions and credits may be taken by a taxpayer by providing that—

> In the case of the death of a taxpayer there shall be allowed as deductions and credits for the taxable period in which falls the date of his death, amounts accrued up to the date of his death (except deductions under section 23 (o)) if not otherwise properly allowable in respect of such period or a prior period.

These two amendments were of course complementary. The overall result is that, for the year of death of a taxpayer who has been on a cash receipts and disbursements basis for federal income tax purposes, outstanding accounts must be reported as income and accrued deductions and credits may be taken except deductions under section 23(o) relating to charitable and other contributions.

The applicability of the amendment to section 42 to physicians was aptly illustrated in a case abstracted in THE JOURNAL on May 24, 1941, page 2426.[1] In that case a physician who was engaged in the practice of medicine in a partnership died,

1. Pfaff et al. v. Commissioner of Internal Revenue, 113 F. (2d) 114, 61 S. Ct. 783.

dissolving the partnership. The agreement under which the partnership operated entitled the deceased physician to share in the book accounts of the partnership to the extent of $27,000, face value. The local collector of internal revenue determined that a fair appraisal of the decedent's interest in the partnership accounts was about one fifth of the face value and that this amount was properly includible as income for the year in which the physician died. The Supreme Court of the United States upheld the collector's determination. The interest of the physician in the outstanding accounts of the partnership was not subject to tax at its face value but on the basis of a fair appraisal of that interest. The local collector of internal revenue undoubtedly took into consideration that some of the accounts were not collectible at all and that others were collectible only in part.

While it may possibly be conceded that the situation that existed prior to 1934 with respect to the taxability of the outstanding accounts of the taxpayer at the time of his death justified remedial legislation, yet the remedy that was devised seems to be unfair to the taxpayer who has been on a cash receipts and disbursements basis. The result is that the income of the taxpayer is built up artificially for the year of death by the inclusion of uncollected accounts—accounts on which the taxpayer did not realize any income whatsoever prior to his death. The ordinary effect of the amendment to section 42 is to subject the taxpayer to higher surtax rates, with a large increase in the amount of income taxes payable for the year of death as compared with preceding years. This increase may readily impose an undue hardship on the estate of the taxpayer to provide sufficient funds to pay the tax.

Whether or not anything can be done to induce Congress to remedy the situation created by the 1934 amendment is still a question. An effort is being made, however, to obtain the enactment of corrective legislation. If section 42 could be amended to make the outstanding accounts on the books of a taxpayer at the time of his death taxable under the federal income tax law as such accounts are collected, rather than taxable as of the date of death of the taxpayer, some relief would be afforded.

Pending possible action by the Congress, several suggestions have been offered as to procedures that a physician may adopt during his lifetime to lighten the income tax load on his estate created by reason of the inclusion of the outstanding accounts as income.[2] Since the effect of section 42 is felt ordinarily by the estate of a physician who has been on a cash receipts and disbursements basis, consideration might be given by a physician to changing over from that basis to an accrual basis during his lifetime. The advisability of effecting such a change, however, is questionable. First, a taxpayer who has been on a cash receipts and disbursements basis cannot change over to an accrual basis without obtaining the consent of the Commissioner of Internal Revenue. Second, a taxpayer on an accrual basis must keep his books in a much more detailed manner than is otherwise required and the procedure for reporting income on that basis is complicated. Also, unless a physician who has been on a cash receipts and disbursements basis arranges to close out all of his outstanding accounts before changing over to the accrual basis, he might be faced with the demand to pay taxes on such outstanding accounts for the year when the change-over is effective and would thus raise the same problems that now arise under section 42, on his death. Omitting from consideration, therefore, any change in the method used by a physician in reporting his income for federal income tax purposes, a physician may during his lifetime to some extent lessen the harsh effects of the amendment to section 42.

A physician should refrain from entering on his books accounts due from patients when the accounts are of doubtful collectibility or known to be uncollectible. The estate may have trouble in proving that an account is bad and in getting an allowance on it, resulting in the payment of income tax on an account which will, in fact, never be collected. A physician should write off known bad accounts at least annually. If bad accounts are carried on the books for years, the estate of the taxpayer will be subjected to the necessity of proving the uncollectibility of the accounts. Such evidence may be difficult to procure. Some physicians follow a practice of entering on their books charges for services rendered to patients who are admittedly charity cases, even though there is no intention to collect or to attempt to collect the charges. Whatever reason a physician may have for doing this, the practice will complicate the duties of the administrator or executor of the estate of the deceased physician who has followed the practice. The administrator or executor may not have any way of determining, from the books of the taxpayer, whether a particular account represents a purely charity case. This will lead to an attempt to arrive at an estimated fair value of the account for income tax purposes, despite the fact that the services were rendered with a definite understanding between the physician and the patient that they were in the category of a charity. Not only may such a practice give rise to misunderstandings between the patient and the estate, but the administrator or executor may have difficulty in convincing the collector of internal revenue of the intent of the physician to omit charge for his services even though a book entry was made indicating a charge.

It has been suggested too that a physician should keep in his files, readily available for use by his estate on his death, all procurable information which will be of aid in making a determination with respect to the collectibility or uncollectibility of an account of a particular patient. Information of this kind may be obtained from the patient or it may come to the notice of the physician from other sources. Finally, if the book accounts of the physician represent a substantial amount, he should anticipate the possibility that on his death a substantial income tax may be payable, by setting aside sufficient cash to take care of the taxes or by providing insurance to cover them. Otherwise the estate may have to be liquidated at a sacrifice to provide the necessary cash to pay the taxes. A physician will therefore do well to consult an attorney or an accountant for the purpose of estimating the amount of such taxes, so that he may make adequate provisions during his lifetime to prevent any unnecessary strain on his estate after his death.

2. Wisconsin M. J. **40**: 1151 (Dec.) 1941.

MEDICAL ECONOMIC ABSTRACTS

CALIFORNIA PHYSICIANS' SERVICE

Two years of experience have brought to light many unforeseen features of the California Physicians' Service. This was inevitable and expected. The board of trustees submitted a report summarizing the experiences and introducing some significant changes in the operation of the plan.[1] At the present time the plan has thirty thousand members. Owing to its pioneer character, this plan could find no pattern on which to base its policy. An abstract of the report follows:

OUR OBJECTIVES

During these past two years we have been trying to do two things: first, to determine the possibility, the cost and the mechanics of administration of an unlimited free choice medical service plan and, second, to run a businesslike operation which would pay the doctor a reasonable fee for his service. We have accomplished the first objective, but only at some sacrifice of the second.

1. California Physicians' Service—Report to Professional Members: Announcement of Changes in Plan, California & West. Med. **55**: 268 (Nov.) 1941.

Under the full coverage contract California Physicians' Service sets no maximum limit on the quantity or quality of care that the doctor may wish to extend, except the limit of one year's treatment in any single illness or injury. This contract was offered to the public as an example of what the medical profession felt that a health service plan should be. It was necessary to determine the change in the habits of people and in their attitudes toward the use of medical service when they had unlimited access thereto.

Our membership of thirty thousand is scattered throughout the state, with representation in every county. This is sufficient to give us an honest sample of experience with California medicine on a free and open access basis.

We must also devise new plans which will produce a more equitable fee for the professional services performed and which, combined with the full coverage plan, will not require a heavy contribution from the profession. This contribution will be relatively small in 1940 and 1941.

Our actual administrative expenses are well below the original maximum set for this purpose, and with increasing volume we can expect still further betterment.

FACTS ESTABLISHED

In our study of the full coverage contract and our experience thereunder, we find certain facts:

1. Our incidence of illness averages better than 17 per cent, that is, almost one fifth of our total membership is under treatment each month. This is much higher than the predictions based on any surveys or other static forms of measurement.

2. The extent of service rendered to these patients is such that, on the average, medical service costs are equal to one unit of service per dues paying member per month. An extremely large part of the services required by beneficiary members is for minor ambulatory illnesses and for chronic conditions.

3. Of the cases under treatment in a single month, nearly 40 per cent are continued from the previous month.

It is a very reasonable assumption that the high frequency of the use of the service, the high proportion of minor illnesses and the dragging on of these cases is the result largely of a complete lack of responsibility on the part of the beneficiary. He need not count cost in any fashion but merely has to present himself to the doctor and ask for whatever may be available.

4. Fifty-six per cent of our membership is composed of women, who require almost 75 per cent of the care extended.

5. Too high a percentage of all membership has been secured in the white collar classes and we have not been able to secure a sufficient percentage in the industrial groups.

These last two items confirm the necessity for our expansion into new fields in order to secure a proper balance of low income members in our service.

6. There does not seem to be any evidence of "chiseling" on the part of professional members to any significant degree. There is no excess of services in any particular district in terms of number of patients treated or in terms of quality of service rendered per patient.

POSSIBLE SOLUTIONS

With these facts in our possession we can plan for betterment. We have three possible solutions: (1) raising dues, (2) inserting some elements of cost sharing, (3) a low cost limited plan.

Item 1 does not propose a very practical solution by itself. Raising dues would no doubt eliminate a considerable number of our present members, and such elimination would be largely among the low income members and not among the higher income members, who have less need for the protection of the service. However, we may do something to raise the unit value without unfairly affecting the membership as a whole. Women require 20 per cent more medical care, in proportion to their number, than the men. It seems reasonable, then, that there should be an adjustment of rates for women to correct this situation.

Item 2 may be the source of considerable betterment. We propose that some responsibility shall be put on the member so that he may feel a share of the burden in direct proportion to his use of the service.

Item 3 is the most important with respect to policy and with respect to actuarial results. The high rate of dues necessary for the full coverage resulted in automatic selection of the "white collar" groups, who were the first to recognize the benefits to be secured through this service. Therefore, in order to correct this, we must now offer a low price plan that will attract the low income and industrial worker.

One of the most important factors we need to balance out the whole is volume, and volume can be secured with safety under limited plans which include only predictable and insurable factors. In this expansion we shall have the benefit of the experience of Eastern and Middle Western medical service associations. These organizations have reported fairly satisfactory experience with this type of contract. They have been able to secure very ready acceptance from the low income industrial groups of these limited service plans. If we can acquire volume under these contracts, it will put us definitely and safely into the low income field. These industrial groups have not been educated to pay for a complete medical service, but, in the experience of other medical service associations, once they have had the limited plan for a reasonable period of time they manifest interest in the broader plans.

Therefore we intend to put forth all of our effort on the acquiring of groups in the industrial field under this type of contract, limiting our acquisition activities in the full coverage plan to the two visit deductible contract only.

CHANGES MADE BY TRUSTEES

The following changes in policy were made at the meeting of the Board of Trustees on September 20:

1. A raise in the dues for women in all new groups effective Oct. 1, 1941, and raises in dues for women in existing groups according to our experience and as the contracts expire.

2. A moratorium on the sale of full coverage contracts, limiting the sale of this service to the two visit deductible contracts only (wherein the member pays the cost of the first two visits).

3. Authorization to the secretary to cancel or modify contracts with existing groups when experience indicates abuse of the service.

4. Authorization to the executive committee to develop means for the inclusion of dependents of the wage earner under the limited surgical plan.

5. Direction to the Acquisition Committee to place all its emphasis on the limited surgical contract in future acquisition.

The question naturally arises as to the over-all effect of these changes. The board of trustees feels that the modification of our full coverage contract and this expansion into new fields will result in the following:

1. We will modify our full coverage plan and we will eliminate unsatisfactory groups.

2. We will reach a new section of the population in the low income industrial groups.

3. We will balance the ideal full coverage with the business-like limited coverage.

4. We will extend our service to the industrial worker and his family, whose need for protection is much greater.

REPORT OF UNITED STATES CHILDREN'S BUREAU ADVISORY COMMITTEE MEETINGS

The Maternal and Child Health and Crippled Children's Advisory Committees of the Children's Bureau met in Washington, D. C., Dec. 1 and 2, 1941, under the chairmanship of Dr. Horton Casparis and Dr. Robin C. Buerki. The two committees met together for the first time this year and included thirty-eight physicians, four dentists, thirteen nurses, four medical social workers, one nutritionist, one physical therapist and one special educator:

Physicians

Fred L. Adair
Carl E. Badgley
S. Josephine Baker
W. W. Bauer
M. O. Bousfield
James Barrett Brown
Robin C. Buerki
Horton Casparis
A. J. Chesley
John S. Coulter
Bronson Crothers
Hester B. Curtis
M. Edward Davis
Robert L. DeNormandie
Eva F. Dodge
Clifford G. Grulee
Henry F. Helmholz
Ruth Jackson
T. Duckett Jones
Albert D. Kaiser
George W. Kosmak
Joseph I. Linde
George M. Lyon
Alice F. Maxwell
Hugh McCulloch
Frank L. McPhail
O. L. Miller
Robert B. Osgood
John R. Paul
Alice N. Pickett
E. D. Plass
Louis Spekter
George S. Stevenson
Clifford Sweet
Felix J. Underwood
Joseph S. Wall
Philip F. Williams
W. C. Williams

Dentists

Floyd H. DeCamp
A. LeRoy Johnson
Guy S. Milberry
Lon W. Morrey

Nurses

M. Corinne Bancroft
Mary P. Billmeyer
Hazel Corbin
Gertrude R. Folendorf
Elizabeth G. Fox
Lalla Mary Goggans
Amelia Grant
Nellie X. Hawkinson
Olivia T. Peterson
Florence L. Phenix
Marion W. Sheahan
Jessie L. Stevenson
Katharine Tucker

Medical Social Workers

Zdenka Buben
Ruth Emerson
Edith I. Epler
Ruth E. Lewis

Nutritionist

Lydia J. Roberts

Physical Therapist

Mildred Elson

Special Educator

Hazel C. McIntire

Many of the administrative problems of these health and medical care programs are closely related. The Divisions of Maternal and Child Health and Crippled Children of the Children's Bureau had been organized July 1, 1941 into a single Division of Health Services under the direction of Dr. Edwin F. Daily.

A progress report of the maternal and child health services throughout the country was presented by Dr. Hart E. Van Riper, assistant director for maternal and child health, Division of Health Services, and a progress report of the Crippled Children Services throughout the nation was presented by Dr. A. L. Van Horn, assistant director for crippled children, Division of Health Services. Copies of these reports may be secured from the Children's Bureau. These reports contain an analysis of state programs involving expenditures last year of $15,664,376 under plans approved by the Children's Bureau.

The medical members of the advisory committees gave special consideration to the qualifications recommended for physicians participating in these programs. Representatives of the American Osteopathic Association were invited to advise the committees concerning the education, training and experience in pediatrics, obstetrics and orthopedics of the members of their professions. The advisory committees of the Children's Bureau after hearing these representatives recommended that the Children's Bureau make no change in its present policy of being guided by the previous recommendations of the advisory committees with respect to qualifications for physicians participating in these programs until a committee appointed by the chairman has an opportunity to study the training and qualifications of osteopathic physicians and report their findings to the Maternal and Child Health and Crippled Children's Advisory Committees of the Children's Bureau for further consideration.

Problems relating to the medical, dental, nursing, medical social and hospital services under the maternal and child health and crippled children's programs were discussed and many recommendations made for future guidance of the Children's Bureau in the administration of these programs. It was recommended that the Children's Bureau appoint a dental consultant to advise with the state agencies on the dental service in both the maternal and child health and crippled children's programs. The need for additional well trained physical therapists was discussed as it related to services for crippled children. The need for the development of child guidance services as a part of the total health program for children was discussed at some length.

Information relating to health and welfare problems of mothers and children in some of the areas most affected by defense activities was presented to the advisory committees. Methods of safeguarding the health and welfare of mothers and children in these areas were discussed and the working relationship of the Children's Bureau with the Office of Civilian Defense and with the Office of Defense, Health and Welfare Services was outlined. Dr. George Baehr, director of the medical service of the Office of Civilian Defense, described the functions of his office in helping various states and localities organize emergency medical services for civilian protection in the event of belligerent action. The work of the joint committee studying the problem of evacuation of civilians in case of need was presented by Dr. Eliot, secretary of the committee.

Major Seeley, executive officer of the Procurement and Assignment Service of the Office of Defense, Health and Welfare Service, presented a report on the development of this new service, which has been created to assist in securing physicians, dentists and veterinarians needed by the military forces and at the same time to protect the civilian population to the greatest possible extent.

The problems of providing health services in the states for minority groups and for nonresidents were outlined and recommendations made to the effect that all children irrespective of race, religion or residence should be given the same consideration.

BRITISH MEDICAL PLANNING

The conference of representatives of the Home Divisions of the British Medical Association was held in London, beginning September 11, through the following day.[1] Representatives were present from nearly all the divisions of Great Britain and northern Ireland. The question of the future organization of the medical profession seems to have dominated the discussion. One speaker spoke on "the chaotic condition of the health services of this country. There was a complete lack of coordination. Government departments vied with each other in efforts at control of various services throughout the country. The lack of order and system involved a very serious wastage of resources, both financial and administrative. Any person or corporation that could produce out of this chaos a comprehensive, well coordinated system of health services would deserve well of the country." He offered a resolution which with slight amendments was adopted and read as follows:

> That in the opinion of this meeting the family and the family doctor of the patient's choice still constitute the primary essential unit in the health services of this country, and that the Medical Planning Commission be invited to regard this as a fundamental principle.

There was much discussion of the extension of medical benefit to a new insurance group and a motion was offered, which was declared out of order, that the insurance practitioners be advised not to undertake this service. A motion was carried complaining that the Insurance Acts Committee had failed to keep local committees adequately informed during the negotiations as to the changes in the insurance conditions. A resolution expressing "complete dissatisfaction with the recent action of the Insurance Acts Committee in its negotiations with the Ministry of Health" was carried by a vote of 71 to 56.

1. Conference of Representatives of Home Divisions, Brit. M. J. Supplement, Sept. 20, 1941, p. 49.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Dr. Austin Acting State Health Officer.—Dr. Burton F. Austin, Montgomery, chief of the bureau of hygiene and nursing of the state department of health, has been appointed acting health officer of Alabama, pending a permanent selection to succeed the late Dr. James N. Baker, Montgomery.

CALIFORNIA

Society News.—Dr. William Edward Chamberlain, Philadelphia, addressed the San Francisco County Medical Society, December 2, on "Role of Fluoroscopy in Medicine."——The Los Angeles Society of Neurology and Psychiatry was addressed, December 17, by Drs. William T. Grant and Leo J. Adelstein on "Quantitative Methods in Neurologic Diagnosis" and "Surgical Treatment of Syringobulbia," respectively. Both are from Los Angeles.

Laboratory for Research in Ophthalmology.—The University of California recently opened a new laboratory to be used for pathology and research in ophthalmology, to be jointly directed by the division of ophthalmology in conjunction with the divisions of ophthalmology and pathology. Dr. Michael J. Hogan, San Francisco, has been made director of the new unit. The laboratory was made possible by a fund of $70,000 known as the Charles Taylor Reeves Foundation, the income from which is to be used in the study of diseases of the eye. Actual construction was accomplished through a donation of Mrs. E. S. Heller.

CONNECTICUT

Changes in Health Officers.—Dr. Thomas J. Bergin, Cos Cob, has been appointed full time health officer of the town of Greenwich.——Dr. Albert E. Childs, Litchfield, has succeeded Elton R. Skilton, as health officer of Morris.——Dr. Philip E. Schwartz has been appointed health officer of Portland, succeeding Dr. John R. Tarrant.——Dr. Ernest R. Pendleton has been appointed health officer of East Granby and Hartland, succeeding, respectively, Adolph Viets and Edward A. Gaylord.

DISTRICT OF COLUMBIA

Course in Aviation Ophthalmology and Medicine.—The George Washington University School of Medicine, Washington, announces a postgraduate course in aviation ophthalmology and aviation medicine, February 5-7. A course in ophthalmology will be held, February 2-4. In the course covering aviation the guest lecturers will be:

Dr. David N. W. Grant, lieutenant colonel, M. C., U. S. Army.
Dr. Frederic H. Thorne, lieutenant colonel, M. C., U. S. Army.
Dr. John M. Hargreaves, major, M. C., U. S. Army.
Dr. Major S. White, major, M. C., U. S. Army.
Dr. John C. Adams, captain, M. C., U. S. Navy.
Dr. Eric Liljencrantz, commander, M. C., U. S. N. R.
Dr. Leon D. Carson, lieutenant commander, M. C., U. S. Navy, Washington, D. C.
Dr. Arnold D. Tuttle, medical director, United Air Lines, Chicago.
Dr. William Hodges McKnight, medical director of American Air Lines, Fort Worth, Texas.
Dr. William Randolph Lovelace II, division of surgery, Mayo Clinic, Rochester, Minn.
Ross A. McFarland, Ph.D., Boston, lieutenant commander, A.-V. (S.) U. S. N. R.

A postgraduate course in ophthalmology will be held, February 2-4. Participating will be Drs. Samuel Hanford McKee, Montreal, Que.; William L. Benedict, Rochester, Minn.; Edwin B. Dunphy, Boston; Harry S. Gradle, Chicago; Meyer Wiener, St. Louis; Algernon B. Reese, New York; Ernest A. W. Sheppard, Washington, D. C.; Avery DeH. Prangen, Rochester, Minn.; William Thornwall Davis, Washington, and Walter I. Lillie, Philadelphia. A course in ocular surgery, pathology and orthoptics is announced for January 26-31. On February 2 the speakers at a meeting of the Washington Ophthalmological Society will be Dr. McKee, on "Routine Examination of the Fundus in Diabetes"; Dr. Reese, "Exophthalmos Associated with Thyroid Disease," and Dr. Wiener, "Reflections on Glaucoma Surgery After Forty Years' Experience."

Society News.—Dr. Herrman L. Blumgart, Boston, discussed "Varieties of Cardiac Pain, Their Clinical and Pathologic Significance," before the Washington Heart Association, November 26.——At a meeting of the Washington Ophthalmological Society, November 3, Dr. Thomas H. Johnson, New York, spoke on neuro-ophthalmology.——Dr. John M. Converse, New York, addressed a meeting of the medical and dental officers of the navy on duty in the District of Columbia and vicinity at the Naval Medical School, December 1, on "Wartime Surgery in England."——The Medical Society of the District of Columbia will devote its meeting, January 21, to a panel discussion on peripheral vascular diseases with Dr. Wallace M. Yater as the moderator. Others participating will include Drs. Norman E. Freeman, Philadelphia; Abram Wilbur Duryee, New York, and James Ross Veal, Washington.

ILLINOIS

Changes in Hospital Superintendents.—Dr. Joseph S. Drabanski has been appointed managing officer of the Chicago State Hospital, succeeding Dr. Edward F. Dombrowski. Dr. John B. Cipriani, Chicago, has been named managing officer of the Illinois Eye and Ear Infirmary, succeeding Dr. Stanley W. Parowski. Dr. James L. Smith, Chicago, became managing officer of the Jacksonville State Hospital on December 1.

Chicago

Course in Electrocardiographic Interpretation.—A course in electrocardiographic interpretation for graduate physicians will be given at Michael Reese Hospital by Dr. Louis N. Katz, director of cardiovascular research. The class will meet each week, starting Wednesday February 18, for twelve weeks, from 7 to 9 p. m. Additional information may be obtained from the Cardiovascular Department, Michael Reese Hospital.

Chicago Tumor Institute Buys Home.—The Chicago Tumor Institute, 21 West Elm Street, announces the purchase of the property where it has been situated since its establishment in 1938. Previously the clinic leased the property. More than 2,000 persons have been treated at the clinic since it opened; one third of the patients were treated free and one third at reduced rates.

Tons of Dust Fall Annually on Chicago.—The smoke abatement department has reported that a monthly average of 55.2 tons of dust per square mile fell last year in Chicago as compared with 54.1 tons in 1940. The downfall of dust at twenty-two stations throughout the city is the measuring stick used to determine the average. May was the dustiest month with 84.3 tons per square mile, compared with 59.6 in the same month in 1940. Increased industrial activity was said to be responsible for much of the 1941 gain. It was also stated that defense activity had forced many Chicago firms to use cheaper grades of coal, which make more smoke unless fired properly. The station located on the top of the building at 33 North La Salle Street, one of two stations down town, had the greatest dust fall, averaging 134.9 tons per square mile monthly. Among the outlying stations the one at 3532 Sheffield Avenue had the highest average with 81.7 tons of dust per square mile monthly. The cleanest outside station, according to the report, was at 1620 West Ninety-Ninth Street with a dust fall of 32.8 tons per square mile monthly.

INDIANA

Appointments to State Board of Health.—Drs. Herman M. Baker, Evansville, and Henry C. Metcalf, Connersville, were recently appointed to the state board of health to succeed Dr. John C. Glackman, Rockport, who resigned several months ago, and Dr. William Wise, Indianapolis. Drs. Ernest Rupel, Indianapolis, and Edmund M. Van Buskirk, Fort Wayne, were reappointed to the board. This is the first time in several months that the board has had a full membership, it is reported.

KANSAS

Health Service Director Goes to Milwaukee.—Dr. Richard F. Boyd, Topeka, who has been director of local health services of the Kansas State Board of Health, recently resigned to become regional medical officer for the Farm Security Administration in Michigan, Wisconsin and Minnesota. He will reside in Milwaukee.

Menninger Foundation Organized. — Announcement is made of the incorporation under the laws of Kansas of the Menninger Foundation, with headquarters in Topeka. The new foundation aims to provide psychiatric education, especially the training of young physicians in psychiatry, to encourage research in psychiatric and psychologic fields; to make available psychiatric treatment for patients in the low income bracket and to prevent mental illness, especially through development of child psychiatry and the application of psychiatric knowledge to education and child rearing. Officers of the foundation are Dr. Karl A. Menninger, president; Mr. John R. Stone, vice president; Dr. William C. Menninger, secretary, and Dr. Robert P. Knight, Topeka, treasurer, and trustees are:

Dr. Winfred Overholser, medical superintendent, St. Elizabeths Hospital, Washington, D. C.
Mrs. Albert Lasker, New York and Chicago.
Dr. John C. Whitehorn, Baltimore.
Mrs. Lucy Stearns McLaughlin, Santa Fe, N. M.
Dr. James Roscoe Miller, Chicago.
Mrs. Sidney C. Borg, New York.
George W. Hite Jr., New York.

Grants have been made for a ten year study of the place of occupational therapy in psychiatric treatment, for a seminar and special Bulletin on Military Psychiatry and the distribution of this information to physicians on the medical advisory boards of the country, and for research in the use of hypnosis in emergency psychotherapy and in substantiating newer psychiatric theories.

KENTUCKY

Changes in Health Officers. — Dr. Jesse M. Dishman, Princeton, health officer of Caldwell County, has been appointed health officer of Fulton County, succeeding Dr. Layson B. Swann, Paducah, who resigned to enter the army.——Dr. Frank L. Lapsley, Shelbyville, has been reelected health officer of Shelby County for a four year term.

Society News. — The Jefferson County Medical Society devoted its meeting in Louisville, December 15, to a symposium on fractures; the speakers were Drs. William Barnett Owen, William McDaniel Ewing, Harry Goldberg, Orville Ray Miller and Robertson O. Joplin, Louisville, and E. C. Hume, D.D.S.——At a meeting of the Louisville Medico-Chirurgical Society on December 12 Dr. Michael J. Henry discussed "Primary Carcinoma of the Liver" and Dr. Laman A. Gray presented a case report on "Extensive Pelvic Endometriosis." Both are of Louisville.

MICHIGAN

State Council of Health.—The governor recently appointed Drs. Harold E. Wisner, Detroit, a member of the state council of health to succeed Dr. Addison D. Aldrich, Houghton; Dr. Oscar D. Stryker, Fremont, was also appointed a member. Dr. Roy C. Perkins, Bay City, was reappointed to the council. Other members are Henry F. Vaughan, Dr.P.H., Ann Arbor, and John A. Galbo, D.D.S., Detroit.

MINNESOTA

Personal. — Dr. Frank J. Hirschboeck, Duluth, has been appointed by the governor a member of the state teachers' college board.——Dr. Cyril M. Smith, Duluth, has been appointed a member of the Minnesota Boxing Commission, his term to run until January 1943.——Dr. Reino H. Puumala, Cloquet, has been named coroner for Carlton County, succeeding the late Dr. Franklin W. S. Raiter, Cloquet, who had served in the position for twenty-five years.——John E. Anderson, Ph.D., director of the child welfare institute, University of Minnesota, Minneapolis, has been appointed chairman of the Minnesota committee of the White House Conference on Children in a Democracy. Dr. Roger L. J. Kennedy, Rochester, has been named a member.

Award First Certificate in Tuberculosis Control Program.—At a ceremony in the Tyler High School Auditorium, Tyler, Dr. Berton J. Branton, Willmar, president of the Minnesota State Medical Association, presented a certificate of accreditation signed by Governor Stassen to M. L. Anderson, Canby, chairman of the board of county commissioners, who accepted it for Lincoln County. The certificate was the first awarded in the cooperative program of the state association and the state department of health to accredit counties showing a tuberculosis mortality rate not to exceed 10 per hundred thousand of population and an incidence of tuberculous infection among seniors in high school not to exceed 15 per cent. The mortality rate must be based on a five year average and the student rate on tests of at least 80 per cent of the senior students of the county. The program is believed to be the first adopted for tuberculosis control in a human population and is patterned after the federal plan to accredit areas showing eradication of tuberculosis in cattle.

MISSISSIPPI

Personal. — Dr. Bert R. Burgoyne, Lake Providence, La., has been appointed superintendent of the South Mississippi Charity Hospital, Laurel, succeeding Dr. John C. Butler, Laurel, who resigned to devote his full time to private practice.—— Dr. Harold H. Rutledge, Richmond, Ky., has been chosen director of the Tate County Health Department.

Society News.—The Delta Medical Society was addressed at its thirty-eighth semiannual meeting at the Hotel Greenville recently in Greenville by Drs. Howard A. Nelson, Greenwood, on "The Patient—His Personality and His Disease"; Otis H. Beck, Greenville, "Urethral Strictures"; Toxey E. Hall, Belzoni, "Subdural Hematoma"; Lawrence L. Beall, Cleveland, "Treatment of Facial Injuries," and Bernard H. Booth, Drew, "Malaria." Dr. Grady W. Reagan, Little Rock, Ark., was the guest speaker, and his subject was "The Medical Treatment of Kidney Infection."

MISSOURI

Dr. Graham Chosen for Lister Lectures.—Dr. Evarts A. Graham, Bixby professor of surgery, Washington University School of Medicine, St. Louis, has been awarded the Lister Medal for 1942, which is given in recognition of distinguished contributions to surgical science, according to *Science*. He will deliver the Lister Memorial Lectures during 1942 or later under the auspices of the Royal College of Surgeons of England.

Society News.—Dr. Albert C. Furstenberg, Ann Arbor, Mich., discussed "Medical Treatment of Ménière's Disease" before the St. Louis Medical Society on November 25. Dr. William Boyd, professor of pathology and bacteriology, University of Toronto Faculty of Medicine, Toronto, spoke before the society, December 2, on "Cause and Effect in Relation to Disease." Dr. James C. Sargent, Milwaukee, lectured before the society on December 16 under the auspices of the St. Louis Urological Society; his subject was "Common Injuries Involving the Urinary Tract."

NEBRASKA

Officers of State Medical Board. —The Nebraska State Board of Examiners in Medicine was reorganized at a meeting, December 10. The following officers were elected: Drs. William R. Boyer, Pawnee City, president; Ernest T. Manning, Omaha, vice president, and Henry J. Lehnhoff, Lincoln.

NEW YORK

New Professor of Anesthesia.—Dr. Paul W. Searles, associate in anesthesia, University of Buffalo School of Medicine, Buffalo, and chief anesthetist in the General Hospital, has been appointed professor of anesthesia and head of the department. He succeeds Dr. John H. Evans, who was elected professor emeritus. Dr. Searles graduated at the University of Minnesota Medical School, Minneapolis, in 1934.

Cancer Institute.—A regional cancer institute will be conducted in Syracuse on January 17 under the auspices of the state medical society, Tumor Clinic Association of the State of New York, Syracuse University College of Medicine and the division of cancer control of the state department of health. Dr. Herman G. Weiskotten, dean of the school of medicine, will open the program, which has been designated a "symposium for practitioners." The speakers will be:

Dr. Bowman C. Crowell, Chicago, Role of the Cancer Clinic in Cancer Control.
Dr. Lloyd F. Craver, New York, The General Practitioner and the Diagnosis of Cancer.
Dr. John J. Morton Jr., Rochester, Advance in Surgical Treatment of Cancer.
Dr. John Howard Ferguson, Syracuse, Biopsy—Indications and Methods.

The evening program will be opened by Dr. Edward S. Godfrey Jr., Albany, state health commissioner; Drs. Guilford Allen Robinson, New York, and Walter T. Murphy, Buffalo, will discuss "Principles of Radium and X-Ray Therapy," and Byrl R. Kirklin, Rochester, Minn., "X-Ray as a Diagnostic Aid in Cancer."

Study of Family Care.—Dr. Frank F. Tallman, clinical director of the Rockland State Hospital, Orangeburg, has been appointed director of the study of parole and family care by the temporary commission on state hospital problems. Central

Islip (N. Y.) State Hospital with an urban population and the Marcy State Hospital, Oneida County, with patients from rural areas were selected for the study, the object of which is to determine to what extent additional psychiatric social work results in increasing paroles and family care. One physician and three social workers have been assigned to Central Islip and one physician and two social workers to Marcy, releasing personnel which can give full time to the study. Dr. Tallman has been granted a leave of absence from the Rockland hospital to devote full time to the work.

New York City

Hospital News.—The City Hospital announced a special lecture to its chest clinic by Dr. Edward D. Churchill, John Homans professor of surgery, Harvard Medical School, Boston, November 12, on "Primary Carcinoma of the Lung."

The Harvey Lecture.—Dr. William C. Stadie, associate professor of research medicine, University of Pennsylvania School of Medicine, will deliver the fourth Harvey Society Lecture of the current series at the New York Academy of Medicine, January 15. His subject will be "Intermediary Metabolism in Diabetes Mellitus."

Dr. Hecht Awarded Medal.—The Frederic Ives Medal of the Optical Society of America was presented on October 24 to Selig Hecht, Ph.D., professor of biophysics at Columbia University, in recognition of "distinguished work in the field of optics," *Science* reports. Kasson S. Gibson, Ph.D., Washington, D. C., president of the society, presented the medal to Dr. Hecht during the twenty-sixth annual meeting of the society in New York. The medal was established in 1928 by Herbert E. Ives, Ph.D., Montclair, N. J., of the Bell Telephone Laboratories, in memory of his father.

Fellowships for Women Physicians.—The Women's Medical Association of the City of New York offers a Mary Putnam Jacobi Fellowship for medical research of $1,000. Available Oct. 1, 1942, the fellowship is open to any woman doctor, either American or foreign, who is a graduate of a reputable medical school. Applications must be filed by March 1 and must be accompanied by statements by persons other than the candidate as to health, educational qualifications and previous work. The applicant should state the problem she proposes to investigate and send her photograph. The recipient of the fellowship will be expected to give full time to her study and make a report for publication on its completion. Application blanks may be obtained from the Mary Putnam Jacobi Fellowship Committee of the association, 321 East Fifteenth Street.

Personal.—Dr. Jacob B. Prager has been appointed medical director of the Israel-Zion Hospital, Brooklyn.——Dr. Jacob M. Gershberg, president of the International and Spanish Speaking Association of Physicians, Dentists and Pharmacists, recently returned from a trip to Mexico and various parts of the United States. He formed new chapters of the international association in Chandler and Phoenix, Ariz., San Diego, Calif., and El Paso and San Antonio, Texas.——The Medical Society of the County of Kings will receive $1,000 and the medical library of the late Dr. Henry Joachim in accordance with a stipulation in his will.——Dr. Thomas A. McGoldrick, Brooklyn, has been appointed chief of the emergency medical service under the U. S. Civilian Defense.——Dr. Joseph Francis McCarthy, professor of urology at the New York Polyclinic Medical School and Hospital, was honored recently when a new wing at the Barros Luco Hospital, Santiago, Chile, was named for him.——The medical and nonmedical staff of Manhattan State Hospital, Wards Island, held a reception there December 8 for Dr. John R. Knapp, chief psychiatrist, who has retired after more than forty-five years' service; recently he has been temporarily serving as acting superintendent. Dr. Knapp was presented with a watch and traveling bag.

Medical Aid for Dependent Children.—Families qualified for aid to dependent children have been included under the medical and nursing service which previously has been available to families on home relief, to veterans and to the blind and aged, according to the New York *Times*. The extension of the service was one of the promised benefits of the merger last July of the board of child welfare with the welfare department of the city. About five thousand physicians representing the medical societies of the city will constitute the panel approved by the medical advisory committee of the welfare department, which is circulating physicians to learn how many wish to respond to aid to dependent children calls. On November 16 about three thousand six hundred had responded affirmatively. They will be paid $2 a visit. There will be fifteen hundred approved pharmacists to whom patients may go for medicine. Bills for medicines will be paid by the welfare department. The number of families classified under aid to dependent children is 22,140; the number of children is 40,690, and the total eligible for the service is about 62,000, it was stated. In case of the aged, the blind and dependent children, the welfare department will be unable to pay attending physicians directly as it does in the case of home relief families. The Social Security Act forbids specific payments and requires that checks be sent to the clients, who cannot be compelled to turn over the cash to the physician. As a result the beneficiaries often do not pay the physician, who in turn has no claim against the welfare department. William Hodson, welfare commissioner, said the Social Security Board was trying to have the law amended.

NORTH CAROLINA

Lectures on Medical History.—Dr. William G. Harrison, Birmingham, Ala., gave a series of public lectures on the history of medicine at the Bowman Gray School of Medicine, Winston-Salem, November 24-28. His topics were "Animal Medicine," "Folklore in Medicine," "The Dawn of Medicine in the East," "Early Greek Medicine" and "Classical Greek Medicine."

Personal.—Dr. Thomas O. Coppedge, Nashville, is now health officer of Nash County.——Dr. Leo B. Skeen, Sanatorium, has been named health officer of Iredell County.——Dr. Vernon W. Taylor Jr., Madison, has been appointed assistant medical director of the city hospital system of Winston-Salem, a position recently created because of an expanded program of public service.

Hospital for Ashe County.—The new twenty-four bed Ashe County Memorial Hospital, Jefferson, was dedicated and formally opened, November 2. The two story stone structure is a WPA project and cost $60,000. Speakers at the dedication included Hon. Frank Dryden, Washington, D. C., acting WPA commissioner; Congressman Robert L. Doughton, Laurel Springs, and Dr. Watson S. Rankin, Charlotte.

NORTH DAKOTA

Sanatorium Superintendent Goes to Seattle.—Dr. Cedric Northrop, superintendent of the state tuberculosis sanatorium at San Haven, has resigned, effective December 1. He plans to accept a position as director of tuberculosis control in the Washington State Department of Health, Seattle, according to the *Journal-Lancet*.

OHIO

Employees Eligible for Retirement to be Examined.—Three physicians were named to a new board to examine city employees of Toledo who have reached the retirement age of 70 but who want their services retained, newspapers reported on December 2. The city council authorized the appointment of the board members on the recommendation of the Academy of Medicine of Toledo and Lucas County. The physicians are Drs. William Frank Maxwell, Claude E. Price and William G. Gardiner. The state legislature ruled some time ago that all employees 70 or older must retire this year. It recently advanced the deadline to the end of 1945 if employees 70 or past can qualify physically to continue working.

Cleveland Health Museum Observes Anniversary.—The Cleveland Museum of Health and Hygiene marked its first anniversary, November 14, at a luncheon held in cooperation with the chamber of commerce. Dr. Victor G. Heiser, New York, spoke on "Toughen Up, America." During the year, thirty-seven thousand persons from forty-four states visited the museum and two hundred and eighty-nine guided tours were conducted through the museum by its staff and volunteer guides from the woman's auxiliary of the Academy of Medicine of Cleveland. The museum has eight hundred and eight members and contributors and is maintained by them and by private subscriptions. Beginning this month the museum will offer three to six month internships in health education; selected applicants will learn how to design, build and install exhibits that effectively teach functions of the body. Dr. Bruno Gebhard, former curator of the Dresden Hygiene Museum, is director of the museum, which was developed as a clearing house for popular health information under the direction of the Academy of Medicine of Cleveland.

OKLAHOMA

Society News.—The Pottawatomie County Medical Society was addressed recently by Dr. William M. Gallaher on "Furuncle of the Nose" and Dr. James M. Byrum, "Some Observations in Obstetrical Surgery." Both are of Shawnee.

Benevolent Fund Committee Named.—The Oklahoma State Medical Association has appointed a special committee to report on the handling of the association's surplus fund for benevolent and other purposes. Members are Drs. Galvin L. Johnson, chairman, Pauls Valley; Robert U. Patterson, dean, University of Oklahoma School of Medicine, Oklahoma City, and George R. Osborn, Tulsa.

Committee to Consider Control of Certain Drugs.—The state medical association has appointed a committee to confer with a committee of the Oklahoma Pharmaceutical Association about regulating the sale of certain drugs which may be a menace to health when used by the public without proper prescriptions. Members of the medical association's committee are Drs. Grady F. Mathews, Oklahoma City, chairman; William Turner Bynum, Chickasha, and Leo J. Starry, Oklahoma City.

Dermatologists Entertain Texas Group.—The Texas Dermatological Association was the guest recently of the Oklahoma Dermatological Association at a meeting at the University Hospital, Oklahoma City. Twenty-two cases for diagnosis and study were presented by Drs. Onis G. Hazel and John H. Lamb, both of Oklahoma City. The group was entertained at a barbecue supper at the country cabin of Dr. Everett S. Lain, Oklahoma City. The Texas association plans to reciprocate at its fall meeting in 1942.

OREGON

Mosquito Eradication Program.—The Works Progress Administration has allocated $131,200 to the state board of health to eradicate mosquitoes in areas adjacent to defense industries and military and naval establishments.

Course in Pediatrics.—The University of Oregon Medical School, Portland, conducted a postgraduate course in pediatrics, December 29-31, for physicians of Oregon and Washington, under the direction of the school's department of pediatrics in cooperation with the divisions of maternal and child health of Oregon and Washington state boards of health. Speakers included Drs. Joseph B. Bilderback, Morris L. Bridgeman, James W. Rosenfeld, Paul V. Woolley Jr., Scott H. Goodnight, Adolph Weinzirl, John A. Gius and Charles E. Gurney.

PENNSYLVANIA

Society News.—The Mercer County Medical Society was addressed in Sharon recently by Dr. John B. Price, Norristown, and John H. Brownback, A.B., professor of biology at Ursinus College, Collegeville, on "Relationship of the Autonomic Nervous System to Upper Respiratory Symptoms" and "Embryology of the Autonomic Nervous System" respectively. ——Dr. Joseph H. Barach, Pittsburgh, addressed the Westmoreland County Medical Society, December 2, on "Diabetes and Its Complications."

Philadelphia

Personal.—Dr. Hubley R. Owen resigned as chairman of the council of defense to give full time to his work as director of public health, effective January 1. Dr. Owen had been serving as defense chairman since last May.

New Chair in Hematology.—The Thomas Drake Martinez Cardeza chair of clinical medicine and hematology has been established at Jefferson Medical College with Dr. Harold Walter Jones, associate professor of medicine at the school, as the first incumbent. The funds were provided by Thomas Drake Martinez Cardeza to carry on the work of the Charlotte Drake Cardeza Foundation for the study and investigation of diseases of the blood and allied conditions. Mr. and Mrs. Cardeza established the foundation in 1938 and have since maintained it in memory of the former's mother. Dr. Jones will continue teaching in the medical college and direct all activities of the foundation. He graduated at Jefferson in 1917.

RHODE ISLAND

Society News.—Dr. James P. Deery, Providence, discussed "Tuberculosis Case Finding at the Army Induction Station" before the Providence Medical Association, December 1, and Dr. Channing C. Simmons, Boston, "Diagnosis of Bone Tumors."

Advisory Council of Health.—Governor McGrath recently appointed Dr. Charles F. Gormly, a vice president of the state medical society, and Mr. John E. Farrell, executive secretary of the Providence Medical Association, as members of the advisory council to the state department of health. Other members of the council are Miss Winifred L. Fitzpatrick, R.N.; Mr. Kenneth D. MacColl, and Dr. Dennett L. Richardson, medical superintendent of the Rhode Island Hospital. All are of Providence.

SOUTH CAROLINA

Clinic Named in Honor of Mill Physician.—The Wood Memorial Clinic was opened in November at the Slater Mill in upper Greenville County. The clinic has been dedicated to the service of the eight hundred families of the textile community and named in honor of the late Dr. Landrum W. Wood, Slater, who for years served there. The unit has an operating room for minor surgical work, dental surgery room, diet kitchen and laboratory. Two beds for convalescence and diagnosis will be added later as the need may arise, newspapers reported.

TEXAS

Personal.—Dr. Jack R. Ewalt, assistant professor of psychiatry at the University of Colorado School of Medicine, Denver, has been named associate professor of neuropsychiatry at the University of Texas School of Medicine, Galveston.—— Dr. Horace A. Baker, Wills Point, has been appointed health officer of Van Zandt County.

Society News.—Dr. Charles H. Warren, among others, addressed the Dallas County Medical Society in Dallas, October 23, on "Sulfanilamide as Prophylaxis in Contaminated Traumatic Wound Cases."——The Texas Pediatric Society held its annual meeting recently in Dallas; officers are Drs. Percy E. Luecke, Dallas, president; Frank H. Lancaster, Houston, president-elect, and John E. Ashby, Dallas, secretary-treasurer. The society will meet in San Antonio in October 1942.

WISCONSIN

District Meeting.—At a meeting of the Ninth Councilor District Medical Society in Wausau, November 13, Drs. Alexander E. Brown, Rochester, spoke on "The Present Day Status of the Sulfonamide Compounds" and Ernest M. Hammes, St. Paul, "Diagnosis and Treatment of Injuries and Diseases of the Spinal Cord."

Dr. Seeger Goes to Texas.—Dr. Stanley J. Seeger, chief of staff of the Milwaukee Children's Hospital and chief of staff of Columbia Hospital, has taken up his residence in Texarkana, Texas. Dr. Seeger has been chairman of the Council on Industrial Health of the American Medical Association since its organization in 1937; he was president of the Medical Society of Milwaukee County in 1926 and of the state medical society in 1933-1934. Texarkana is Mrs. Seeger's former home.

Personal.—Dr. George M. Shinners, Green Bay, has been appointed health commissioner of Green Bay.——Dr. Charles D. Boyd, Kaukauna, was guest of honor at a banquet recently, marking his completion of fifty years' practice in the community. ——Dr. Elmer L. Sevringhaus, Madison, has been elected an honorary foreign member of the National Academy of Medicine of Buenos Aires. Dr. Sevringhaus toured South America early this year under a government travel grant.——Dr. Willard M. Sonnenburg, Sheboygan, was recently elected president of the Sheboygan County Conservation Alliance.

GENERAL

Another Fraudulent Solicitor.—The National Publishers Association, New York, announces that a fraudulent magazine solicitor using the names J. R. Hamilton, J. S. Stewart and C. O. Reed has been calling on physicians exclusively, offering subscriptions to *Newsweek* featuring a "special publicity offer —40 issues *Newsweek*." This man issues a green store receipt bearing the offer in a rubber-stamp imprint and also rubber-stamps "Newsweek, 152 West 42nd St., New York City." He pockets full amount of his collections, making no report of the orders. Physicians approached by this solicitor are urged to notify the police and ask them to wire the National Publishers Association, 232 Madison Avenue, New York, collect. The fraudulent representative's description is: age 40 years, height 5 feet 10 inches, weight about 175 pounds; he has brown eyes and black hair.

National Academy of Sciences Closes Building to Public.—Because of the large amount of work being done by the National Academy of Sciences and National Research Council committees in an advisory capacity to the government during the present emergency, and because exhibit and other rooms formerly open to the public are now occupied as offices, the Council of the National Academy of Sciences has directed the National Academy of Sciences Building be closed to the public until further notice. The academy regrets that this step is necessary but will, as soon as circumstances permit, reinstal exhibits of scientific interest to the public. The annual meeting of the academy will be held in the academy building, April 27-29, but attendance, formerly open to the public, will be limited to academy members, their invited guests, the press and to nonmembers who present papers before the academy. Only members of the academy and of the press will receive abstracts of papers.

Extensive Survey of Eye Injuries in Industry.—A report has just been issued of a study of eye injuries in industry which was sponsored by the National Society for the Prevention of Blindness. The report, prepared by the late Louis Resnick, industrial relations director of the society, is based on two decades of personal observations in workshops throughout the country and contains a complete summary of eye hazards existing in American industry today. According to the study, about three hundred thousand eye injuries occur in factories, mills, mines and workshops each year. Of the thousand eye injuries expected to occur each day, all but twenty could be prevented, it was said. There are in the United States more than eighty thousand persons who have lost the sight of one eye as a result of industrial hazards and close to eight thousand who have lost the sight of both eyes; the number of persons who have lost permanently part of the vision of one or both eyes undoubtedly runs into hundreds of thousands. These are conservative estimates and since many factors are involved in accurate reporting, the survey points out that the injuries considered represent only a part of the total number which actually occur. Eye injuries lead to the loss of more than fifty-three million man hours of work yearly, the report states. Discussing the compensation for such injuries, the report shows that in liberal states the maximum compensation paid for total loss of vision is two thirds of the wage received by the injured workman at the time of the accident, whereas in some states, as in Oregon, the maximum compensation for total loss of vision is as low as $30 a month for life. Great financial loss to the workman and the employer could be averted by the cooperation of the two groups in the utilization of demonstrated methods of preventing accidents and diseases.

HAWAII

Dr. Wayson Completes Fifty Years in Medicine.—Dr. James T. Wayson, who from 1918 to 1931 was general health officer of the Territory of Hawaii, Honolulu, recently completed fifty years in the practice of medicine. A few years after his graduation at the University of California Medical School, San Francisco, Dr. Wayson went to Hawaii, where he was at one time physician in charge of the Kalihi Boys' Home and superintendent of the Kapiolani Girls' Home, Honolulu. He was city and county physician of Honolulu from 1911 to 1918. Since 1932 he has been physician to the Board of Leper Hospitals. He has served as a member of the territorial board of health and of the board of medical examiners for several terms. Dr. Wayson, a native of Port Townsend, Wash., is 71 years of age.

CORRECTIONS

Transfusion of Blood and Blood Substitutes.—In an editorial under this title in THE JOURNAL, Nov. 8, 1941, page 1627, in the last paragraph seven lines from the end is the statement "One thousand cc. of plasma gives 8 cc. of dried product." This should have read "One hundred cc. of plasma gives 8 cc. of dried product."

Sodium Lactate in Distilled Water.—In the clinical note by Quick and Lord entitled "Acute Hemolytic Anemia Following Sulfathiazole Administration" in THE JOURNAL, Nov. 15, 1941, page 1704, the authors state that they used "infusions of sodium lactate—Ringer's solution." This was an error and should have been "infusion of sodium lactate in distilled water."

Government Services

Committee for Vocational Rehabilitation

A special committee representing federal agencies concerned with the vocational rehabilitation of war veterans and civilians was appointed on Dec. 22, 1941, by Paul V. McNutt, federal security administrator, according to the New York *Times*. It is planned to draft a program of rehabilitation to meet the current and postwar suffering. The committee membership includes Watson Miller, assistant federal security administrator, chairman, and representatives of the Office of Production Management, the Social Security Board, the Veterans Administration, the Public Health Service, the Employees Compensation Commission, the Department of Labor and the Office of Education. The *Times* reported that both organized labor and industrial management are to be approached for advice and cooperation.

Hoff Hall at Army Field Service School

Hoff Hall, the new academic building of the Medical Field Service School at Carlisle Barracks, Pa., was formally accepted by the acting commandant of the school on November 12. It is a two and one-half story stone structure costing $350,000. The building contains an auditorium with seating capacity for four hundred persons and facilities for sound pictures and for instructional aid. There are two classrooms each with a capacity for four hundred persons and an air conditioned library. In addition there are smaller classrooms, offices, and a museum.

Hoff Hall.

Hoff Hall is built of native limestone quarried partly on the military reservation and is faced with Vermont granite. It is named for the late Col. John Van Rensselaer Hoff, a distinguished officer of the medical corps and leader in the movement by which the medical department became a staff corps. He graduated at Albany (N. Y.) Medical College in 1871 and at the College of Physicians and Surgeons in the City of New York in 1874. In the same year he was appointed first lieutenant and assistant surgeon, U. S. Army. He organized the first detachment of the hospital corps in the army at Fort Reno, Indian Territory, and the first company of instruction hospital corps at Fort Riley, Kan., in 1891. He was recommended for a medal of honor in the Sioux campaign in 1890 and 1891. He served through the war with Spain as chief surgeon in Puerto Rico, was chief surgeon of the China relief expedition in 1900 and was a member of the faculty of the Army Medical School in 1901 and 1902. In 1905 he was commissioned assistant surgeon general and in that year was detailed observer with the Russian army in the Russo-Japanese War; from 1910 until retirement for age in 1912 he was chief surgeon of the Department of the East. Colonel Hoff was a pioneer in the training of enlisted men of the medical department. He insisted that the medical soldier is as much a soldier as any other and must receive adequate drill, and training. His ideas have prevailed. At the recent exercises Col. Edgar E. Hume, acting commandant, received the key to the building from the constructing quartermaster, Lieut. Col. Jacob Osterman.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 22, 1941.

Food in Case of Invasion and Heavy Bombing

The minister of food has announced plans to secure an orderly distribution of food in the event of invasion. In threatened districts food shops would be closed—probably for a few hours—to permit rapid stock taking so that the voluntary food officers would know precisely what food was available and be in a position, with the help of military advice, to decide what amounts would be distributed to each person. Reserves of food in bulk belonging to the ministry vary from district to district, according to military advice. Householders are told that the quantity of food stored for an emergency should be one week's or at most two weeks' supply. Plans for emergency feeding on a wide scale in London have been made by the county council in case heavy bombing of the capital is resumed. Catering establishments of all kinds—hotels and workmen's dining rooms, clubs, teashops, taverns and milk bars—have all been brought in and, where practicable, industrial canteens also will assist. These plans will be put into force only when the authorities consider the emergency to be really grave and only in those parts of the capital where damage to buildings, gas, electricity, water and transport services make emergency feeding essential. Given such conditions, three hundred voluntary officials stand ready to organize a meals service for any emergency. Standard menus will be arranged. Tea will be available at 2 cents a cup, milk at 4 cents a glass, soup (pea or vegetable) at 4 cents a mug, rice pudding for children under 5 at 5 cents a plate, milk soup with bread for children under 5 at 12 cents a mug, meat and vegetable stew with bread 12 cents a plate, meat and vegetables at 18 cents. People will be asked to take with them to these feeding centers their own dishes and cutlery and will be told that basins and mugs are better than plates and cups. If a district is badly bombed but the conditions do not warrant the operation of emergency plans, local caterers will be able to call for supplies of hot stew in bulk from establishments equipped for big scale production.

Destruction at Museum of Royal College of Surgeons

Largely irreparable damage was done by German bombs to the greatest pathologic and anatomic museum in the world. Sir St. Clair Thomson has made a report on the specimens illustrating the surgery of the ear, nose and throat. For many years the museum assembled these specimens and received from eminent specialists invaluable collections representing their life work. One of the earliest gifts of normal anatomy was received from the aurist Toynbee, who presented his 300 specimens of the anatomy of the temporal bone. This addition was greatly enriched when Arthur Cheatle presented his unrivaled series of sections of the temporal bone. Both these collections have been severely damaged. The basis of the rhinologic section of the museum was secured when the British obtained the large collection made by Onodi of Budapest illustrating the anatomy of the nose and accessory sinuses. It has been heavily damaged, but about 95 specimens are intact and the others can be replaced, as they represent normal anatomy. The 14 specimens of the anatomy of the paranasal sinuses recently presented by the late Professor Hajek are intact. He was able to escape from Vienna about two years ago and with the generous help of American and British colleagues reached London. Here through the help of his confrères he spent his last two years, during which time he enjoyed the liberty which he so much appreciated. When he escaped from Vienna, he and his wife had their gold watches taken from them and he was allowed to bring only money equivalent to $2.50. Yet he managed to bring 14 specimens of his collection of rare irregularities of the anatomy of the nasal sinuses. The rest of his 150 specimens had to be left in Austria. The 14 formed part of the specimens he had shown during fifty years to his classes. As a token of his gratitude for deliverance from the city in which he had long been a famous teacher he presented the specimens. The valuable addition to the museum by V. E. Negus of the specimens forming the foundation of his classic study on the comparative anatomy and physiology of the larynx has escaped damage.

International Standard for Vitamin E

An international standard for vitamin E has been established. As for vitamins A, B, C and D the National Institute of Medical Research, London, acting on behalf of the Health organization of the League of Nations, has undertaken its supply to laboratories and research workers throughout the world. Synthetic racemic alpha tocopherol acetate has been adopted as the international standard for the vitamin. Investigation of its chemical, physical and biologic properties, its suitability as an international standard and its application in biologic assay was performed at the request of the Health Organization of the League of Nations by the vitamin E subcommittee of the accessory food factors committee of the Lister Institute and the Medical Research Council. The subcommittee obtained the cooperation of experts in fourteen laboratories in Europe and America. It recommends that the international unit for vitamin E should be defined as the specific activity of 1 mg. of the standard preparation. This is the average amount, administered by mouth, which prevents resorption gestation in rats deprived of vitamin E.

In normal times the results of the cooperative investigation would have been submitted for discussion at the third international conference on vitamin standardization, which had been arranged for the autumn of 1939, but because of the war it was not held. However, the recommendations have been placed before the members available of the League of Nations Permanent Committee on Biological Standardization and the International Conference on Vitamin Standardization. These have taken the responsibility of adopting the proposed standard, definition of the international unit and the authorizing of the National Institute of Medical Research to proceed with the distribution of the standard. This is issued as a solution in olive oil of the strength of 0.1 Gm. containing 1 international unit. In countries with national control centers it will be supplied to their directors for distribution. It will also be supplied to laboratories and research workers in Britain and in countries where national control centers have not yet been set up. Applications should be made to the Department of Biological Standards, National Institute for Medical Research, Hampstead, London, N.W. 3.

Control of the Sale of Nostrums

The Pharmacy and Medicines Act of 1941 stringently controls the sale of secret remedies. The Ministry of Health has now issued a circular to the food and drug authorities drawing their attention to the power conferred on them to prohibit the advertisements calculated to lead to the use of articles for the treatment of Bright's disease, cataract, diabetes, epilepsy or fits, glaucoma, locomotor ataxia, paralysis or tuberculosis. Similar power is conferred in relation to articles for procuring miscarriage. The act further makes compulsory the disclosure by appropriate means of the composition of medicines sold by retail other than when prescribed, made up and supplied for a particular person. Because of the war, the enforcement of the last provision is postponed until July 1942.

RIO DE JANEIRO

(From Our Regular Correspondent)

Dec. 22, 1941.

Typhus Fever in Brazil

Since 1929 Lemos Monteiro of the Butantan Institute has ascertained by laboratory procedures the existence of several cases of a typhus-like rickettsiosis in the state of São Paulo. In 1932 he demonstrated with the collaboration of Parker and Davis and of Dyer of the United States by cross immunization that São Paulo typhus and Rocky Mountain spotted fever are identical. In 1934 J. A. Moreira and Octavio Magalhaes reported a few cases of typhus in the state of Minas Gerais, and in 1939 J. Travassos and E. Dias of the Oswaldo Cruz Institute proved experimentally that Minas Gerais typhus and Rocky Mountain spotted fever are identical too. Now Drs. J. Tostes and G. Bretz have reported for the first time, in a rural section of the state of Rio de Janeiro, a small outbreak of a disease that, from the clinical, epidemiologic and experimental standpoints is very similar to the Rocky Mountain spotted fever that is known to occur in the states of São Paulo and Minas Gerais. The rickettsial nature of the disease was well established through the peritoneal inoculation in guinea pigs of blood from the patients suffering from the infection. In the opinion of the authors the picture presented by the animals shows a close relationship between the Rio de Janeiro virus and that of Rocky Mountain spotted fever. The incubation time varies from two to six days. The animals show high fever (40-41 C., or 104-105.8 F.) and about 85 per cent die around the end of the first week. A high percentage of male guinea pigs develop scrotal reaction followed frequently by necrosis of the scrotum. The blood is infective during the period of high fever, reproducing the disease when inoculated in other animals. The brain shows a high virus concentration and, stored at a low temperature (—4 C.) is used for reinoculations. The most important finding at autopsy is the enlarged and darkened spleen. It is also frequent to find enlarged lymph nodes and swelling of the subcutaneous connective tissue. The rickettsias are usually found in the endothelial cells of the peritoneal sheet. The Weil-Felix reaction with Proteus 0 x 19 was positive in 5 out of 6 patients examined. The authors have made extensive researches to discover the vector of the disease. The experiment with ticks of the infected area have given till now negative results. The identification of the virus is still incomplete, but the authors are inclined to think that the virus is of the São Paulo and the Minas Gerais strains, and so of western Rocky Mountain spotted fever as well.

The Yellow Fever Situation

In all Brazil as in the whole Western Hemisphere there have been no reports of cases of yellow fever of the urban type during 1941 and in the previous three years as well. Credit must go to those who have perfected control methods so successfully begun in this hemisphere by Gorgas and Oswaldo Cruz. Attention now centers on jungle yellow fever, which is the same disease as urban yellow fever, but with this distinguishing epidemiologic characteristic that in its special forest environment it is not transmitted by Aedes aegypti. Risk of yellow fever epidemics will remain as long as the jungle type of the disease persists. During the year 1941 antiaegypti measures have been intensified throughout large areas and many additional districts are now apparently free from this mosquito. There have been advances in the detection of yellow fever, and this point is very important as the failure to suspect the disease has caused the loss of valuable time in the past. It is no longer sufficient to accept the opinion of the clinician, even experienced. Happily the laboratory is now able to give conclusive information, even in clinically mild or quite atypical cases, through viscerotomy and protection tests. During the past epidemic season 149 viscerotomy proved cases occurred in rural sections of the states of Rio de Janeiro (4) and Espirito Santo (145). Vaccination was continued on a large scale, the total since the beginning of the use of the procedure almost reaching 2 million vaccinations. Some time during the year 1940 it became apparent that the vaccine being used was not adequately protecting the inoculated persons against the infection, and the fact has been confirmed by postvaccination protection tests. The vaccination effort was reduced while studies were being made to determine the causes of the failure. Fortunately the difficulties in the preparation of a suitable vaccine have been overcome and results comparable to those reported previously were once more obtained. According to the new distribution of tasks, since the reorganization of the federal department of health reported in a previous letter (THE JOURNAL, July 12, 1941, p. 132) the yellow fever service of the department has assumed full responsibility for the antiaegypti work, for the viscerotomy and for field vaccination, while the International Health Board of the Rockefeller Foundation continues to cooperate in the epidemiologic and laboratory studies of the disease and in the preparation of vaccine.

Progress in the Pharmaceutical Industry

The chemical-pharmaceutical industry has been in full development in Brazil, since the beginning of World War II. In 1940 the drug and pharmaceutical products took second place, by value, among the exported manufactured goods. At the head of the list are the medicinal oils and emulsions, as well as aqueous and alcoholic extracts of medicinal plants, the last ones forming an important field, as the flora of Brazil is very diversified and rich. The increase over the year 1939 represents more than 400 per cent. Mexico, Peru and Colombia, in this order, are the countries that imported most from Brazil in the field of drugs and medicinal preparations. A very recent development in this field is the report, from the chemical laboratory of the Department of Agriculture, that the liver of "cação"—Mustelus vulgaris—a large sharklike fish commonly found off the coast of northern Brazil, is rich in vitamin A. The analysis demonstrated an average potency of about 20,000 international units per gram.

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 15, 1941.

Loan for Health Department in Chile

The government of Chile has received the approval of the parliament for a loan of 500 million Chilean pesos ($20,000,000) for public health work, more especially for the construction of hospitals, works of sanitation, mother and child protection, a campaign against venereal diseases and tuberculosis and finally the industrialization of lands. Chile has perhaps the highest mortality rate in the world. The morbidity is likewise shockingly high, particularly as regards tuberculosis, syphilis and infectious diseases. These influences incapacitate 20 per cent of the population for working. Chile has a shortage of twenty thousand hospital beds. The obstetric facilities cannot accommodate even 60 per cent of the parturient women. Patients with mental diseases are inadequately provided for. Hospitals of from twenty-five to two hundred and forty beds are urgently required in twenty-eight cities, and insane asylums need equipment. This will require 300 million Chilean pesos ($12,000,000).

The infant mortality is enormous, as is the number of illegitimate children, forty thousand of whom are without parents. Only 30 per cent of the population live in hygienically unobjectionable towns and 56 per cent in localities which have no hygienic facilities whatever. Of the vegetables marketed in

Santiago de Chile, 80 per cent have been fertilized with sewage. To remedy this situation, sewerage systems must be installed in one hundred and seventy localities and drinking water must be provided for seventy-four. The expenses involved in this are estimated at 90 million Chilean pesos ($3,600,000). The country has 400,000 syphilitic patients. Facilities for hospitalization, treatment, isolation and education of these patients are urgently needed. The expenses involved are estimated at 90 million Chilean pesos. Chile has about 200,000 tuberculous patients with a mortality of 400 per hundred thousand of the population. There is a shortage of six thousand beds for tuberculous patients. An efficient campaign against tuberculosis will require 100 million Chilean pesos ($4,000,000).

Menarche in Buenos Aires

Dr. Halperín Pines recently sought to determine the question of the age at which girls in Buenos Aires first menstruate by examining 10,710 Argentine, Spanish and Italian girls in the population. The results are given in the following tabulation:

Age at Initial Menstruation	No. of Cases	Per Cent
9	28	0.2
10	156	1.45
11	955	8.9
12	2,011	18.7
13	3,142	29.5
14	2,456	22.9
15	1,192	11.7
16	456	4.2
17	204	1.9
18	90	0.8
19	20	0.1

In 1 case menstruation set in at 7 years, in 3 cases at 8 years and in 3 at 20 years. In the majority of cases, accordingly, menstruation began with the thirteenth year. In a similar study, made by Ries and Bueno of 2,947 Argentine children in 1935, age 14 was found to be the initial age of menstruation in most of them. A further analysis was made of 886 Argentine children, most of them belonging to the best social levels. This study gave the following statistical picture:

Age at Menstruation	No. of Cases	Per Cent
8	1	0.11
9	5	0.56
10	33	3.7
11	170	19.1
12	205	28.2
13	253	28.4
14	121	13.6
15	34	3.8
16	10	1.1
17	8	0.9
18	...	...
19	1	0.1

These figures indicate that menstruation sets in at an earlier age in girls in the economically higher brackets.

The Spanish children belonging to the poorer classes begin to menstruate most frequently when 14 and 15 years old, at an age later than that of Argentine and Italian girls in the population. Among these, menstruation sets in in Italian girls mostly at the thirteenth and fourteenth year age level.

News

The Rockefeller Foundation has granted to the physiologic institute of the university of Córdoba $1,500 for the purchase of apparatus and animals for studies on the physiology of the sex life of South American monkeys.

Chile has established the Servicio Nacional de Salubridad Pública, which is to control all sanitary organizations that are concerned with prophylaxis and health protection. The new organization will take over a great part of the activity which hitherto was handled by the cities, particularly in the control of foodstuffs, in the health inspection of housing facilities, industries and so on.

A Buenos Aires firm (Iturrat) has donated 20,000 pesos ($6,000) for the department of tuberculosis in the university of Buenos Aires to be used to support social work.

At the suggestion of the director of the Instituto Osvaldo Cruz in Rio de Janeiro, Dr. César Pinto, it has been planned to found a Sociedad Internacional contra la Hidatosis. A meeting of Argentine, Brazilian and Uruguayan physicians will be held in Uruguay to promote this matter.

The council of the University of Buenos Aires, in agreement with the faculty of medicine, has decided to celebrate the "Dia del Medico" every year on October 18.

The faculty of medicine of the University of Buenos Aires has decided to create a bureau which is to cultivate relations with American universities. This organization is connected with the dean's office and is to maintain close scientific, administrative and scholastic relationships with all faculties of medicine of the three Americas.

Prof. Juan Ramón Beltrán, professor of medical history in Buenos Aires, at the invitation of the faculty of medicine of Rio de Janeiro, is giving a series of lectures in Rio de Janeiro on medicine in ancient Greece.

Dr. Alvaro E. Bence received from the Asociación Argentina para el Progreso de las Ciencias a stipend for the study of bronchoscopy with Chevalier L. Jackson and Louis Clerf in Philadelphia.

Dr. Pedro Belou, professor of anatomy in the faculty of medicine of Buenos Aires, will lecture during the coming months in the leading cities of the South and Central American countries in behalf of Pan American medical solidarity. He has also been invited by several universities in the United States. While in this country he is planning to have English adaptations made of scientific films on neuraxis and the arterial system.

Deaths

Dr. Benigno T. Escobar, professor of clinical surgery at the faculty of medicine of the University of Asunción, Paraguay, aged 63, died in Buenos Aires, where he was conducting studies.

Prof. Dr. Alejandro Centeno, internist at the faculty of medicine of the University of Córdoba, Argentina, died recently.

Marriages

ROBERT VAN ZANDT BUCKLIN, Evanston, Ill., to Miss Rosemary Leonore Heiny in Tacoma, Wash., in October 1941.

JAMES LUTHER SPENCER JR. to Miss Frances Elizabeth League, both of Charleston, S. C., Sept. 27, 1941.

CARL T. BUEHLER JR., Halstead, Kan., to Miss Maxine James of Burlington Junction, Mo., in September 1941.

WILLIAM HUBBARD GRIMES JR., Colquitt, Ga., to Miss Claire Rosalinde Richards of Atlanta, Sept. 20, 1941.

DAVID SHIELDS CARROLL, Morristown, Tenn., to Miss Mary Kathryn McGuire of Memphis, Nov. 8, 1941.

NORMAN W. HENRY JR., Mooresville, N. C., to Miss Ethel R. Black of Vineland, N. J., Aug. 28, 1941.

KARL E. JOHNSON, San Diego, to Miss Catharine M. Harris of Santa Barbara, Calif., Sept. 20, 1941.

MCLEMORE BIRDSONG, Charlottesville, Va., to Miss Charlotte Spain of Petersburg in October 1941.

ARNOLD F. STRAUSS to Miss Marjory Ware Spindle, both of Norfolk, Va., in October 1941.

HERBERT HOLDEN THOMAS, Huntsville, Ala., to Miss Louise Petry of Eufaula, Sept. 1, 1941.

JAMES F. LYONS, Miami, Fla., to Miss Patricia Semple of Coral Gables in August 1941.

Deaths

Walter Lindsay Niles ✠ New York; Cornell University Medical College, New York, 1902; since 1916 professor of clinical medicine and from 1919 to 1928 dean, and since October 1941 acting dean, at his alma mater; member of the Association of American Physicians and the American Clinical and Climatological Association; vice president of the New York Academy of Medicine from 1934 to 1936, on the board of trustees from 1928 to 1932 and again since 1936 and chairman since 1937; member of the Joint Administrative Board of New York Hospital, Cornell Medical College Association; attending physician, New York Hospital; consulting physician, Southampton (N. Y.) Hospital, Jamaica (N. Y.) Hospital, Nassau Hospital, Mineola; Bellevue Hospital, New York Infirmary for Women and Children, and Memorial Hospital; author of the chapter on intestinal diseases in Cecil's Medicine; aged 63; died, Dec. 22, 1941, of cerebral hemorrhage.

Adam Gillespie Nichol, Nashville, Tenn.; University of Nashville Medical Department, 1898; member of the Tennessee State Medical Association, Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; formerly assistant professor of orthopedic surgery at the Vanderbilt University School of Medicine and assistant professor of operative surgery at his alma mater; for many years on the staff of the Nashville General Hospital; member of the board of trustees of the Davidson County Tuberculosis Hospital; member of the advisory board of the Junior League Home for Crippled Children, formerly known as the Convalescent Home for Crippled Children, of which he was head of the staff; aged 65; died, Nov. 14, 1941, in Dallas, Texas, of cerebral hemorrhage.

Marius Liborius Abbene, Brooklyn; New York Homeopathic Medical College and Flower Hospital, New York, 1914; member of the Medical Society of the State of New York; fellow of the American College of Surgeons; instructor of obstetrics and gynecology at the Long Island College of Medicine; obstetrician, Bushwick Hospital; associate gynecologist and obstetrician, St. Mary's Hospital; associate gynecologist and obstetrician, and chief, gynecological and obstetrical clinic, Greenpoint Hospital; physician for the local draft board in the first and second world wars; aged 55; died, Dec. 9, 1941, of coronary thrombosis.

Casper Walker Jennings, Greensboro, N. C.; Medical College of Virginia, Richmond, 1916; member of the Medical Society of the State of North Carolina and the American Academy of Ophthalmology and Otolaryngology; formerly secretary of the Guilford County Medical Society; past president and secretary of the North Carolina Eye, Ear, Nose and Throat Society; on the staffs of the Wesley Long Hospital, St. Leo's Hospital, Sternberger Hospital for Women and Children, and Piedmont Memorial Hospital; aged 48; died, Nov. 22, 1941, of acute dilatation of the heart.

Greer Baughman ✠ Richmond, Va.; Medical College of Virginia, Richmond, 1897; professor of obstetrics at his alma mater; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons and the Southern Surgical Association; fellow of the American College of Surgeons; visiting obstetrician, Stuart Circle Hospital; consulting obstetrician, Memorial and St. Philip hospitals; formerly surgeon to the fire department of Richmond; aged 67; died, Dec. 2, 1941, of chronic nephritis and uremia.

Eugene John Bozsan ✠ New York; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1913; member of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; served with the Austrian-Hungarian Army during the World War; on the staffs of the Hospital for Joint Diseases and the Morrisania City Hospital; aged 51; died, Dec. 4, 1941.

Hampton Pierson Howell ✠ New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1894; member of the American Laryngological, Rhinological and Otological Society; attending otolaryngologist of the Roosevelt Hospital from 1929 to 1934 and consultant otolaryngologist since 1935; aged 71; died, Dec. 11, 1941, at his home in Westhampton Beach, N. Y.

Jesse Bundren Helm ✠ Medical Director, Captain, United States Navy, Washington, D. C.; University of Louisville (Ky.) Medical Department, 1911; fellow of the American College of Physicians; entered the naval service July 20, 1913 and was retired on Aug. 1, 1940 for disability incurred in the line of duty; aged 56; died, Nov. 26, 1941, in the Garfield Hospital of hypertensive heart disease.

Maurice Schneider, Chicago; Northwestern University Medical School, Chicago, 1928; was a member of the associate staff of the teaching faculty of the Cook County Graduate School of Medicine, in the division of diseases of children; associate on the staff of the Cook County Children's Hospital; aged 38; died, Dec. 2, 1941, in the Mount Sinai Hospital.

Henry Farrer Owsley, Poughkeepsie, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1896; veteran of the Spanish-American War; aged 70; died, Nov. 27, 1941, in the Westchester Division of the New York Hospital, White Plains, of bronchopneumonia and arteriosclerosis.

Henry Ernest Paul, Toronto, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1901; member of the American Urological Association; served during the World War; aged 65; on the staffs of the Christie Street Hospital and St. Joseph's Hospital, where he died, Nov. 7, 1941.

George Wallace Elliott, Vancouver, B. C., Canada; Manitoba Medical College, Winnipeg, 1899; formerly member of the Winnipeg police force; at one time medical immigration officer of the Canadian government at Ellis Island, N. Y., and at Portland, Maine; aged 77; died, Oct. 21, 1941

George Edwin Shetrone, Shillington, Pa.; Hahnemann Medical College and Hospital, Philadelphia, 1921; member of the Medical Society of the State of Pennsylvania; physician for the county schools; on the staff of the Homeopathic Hospital, Reading; aged 43; died, Nov. 6, 1941.

John Trantham Stephenson, Emmett, W. Va.; University of Georgia Medical Department, Augusta, 1925; member of the West Virginia State Medical Association; served during the World War; formerly a physician in the Indian Service; aged 53; died, Nov. 14, 1941.

James Tilden Christian, Sacramento, Calif.; Cooper Medical College, San Francisco, 1902; member of the California Medical Association; formerly county health officer; served during the World War; aged 63; died, Nov. 30, 1941, in a hospital at San Francisco.

Charles Ashton Webster, Yarmouth, N. S., Canada; College of Physicians and Surgeons, medical department of Columbia College, New York, 1886; fellow of the American College of Surgeons; visiting surgeon, Yarmouth Hospital; aged 77; died, Nov. 22, 1941.

John Hill Hammond ✠ La Fayette, Ga.; Jefferson Medical College of Philadelphia, 1883; an Affiliate Fellow of the American Medical Association; for many years chairman of the city board of education; formerly county health commissioner; aged 85; died, Nov. 26, 1941.

James A. Dorsett, Lucedale, Miss.; Atlanta (Ga.) College of Physicians and Surgeons, 1902; member of the Mississippi State Medical Association; at one time mayor of Lucedale; aged 64; died, Nov. 5, 1941, in the Mobile Infirmary, Mobile, Ala.

Henry Hunt Duke, Denair, Calif.; Hospital College of Medicine, Louisville, Ky., 1899; formerly passed assistant surgeon in the United States Public Health Service Reserve; veteran of the Spanish-American and World wars; aged 68; died, Oct. 11, 1941.

Allen Hanson Blake ✠ Somerville, Mass.; Harvard Medical School, Boston, 1904; member of the New England Roentgen Ray Society and the Radiological Society of North America, Inc., on the staff of the Somerville Hospital; aged 60; died, Dec. 9, 1941.

James Eugene Dwyer, Milwaukee; University of Maryland School of Medicine, Baltimore, 1905; served during the World War; aged 64; on the staff of the Veterans Administration Facility, where he died, Nov. 14, 1941, of nephrosclerosis.

William Otto Bailey, East Orange, N. J.; Eclectic Medical College of the City of New York, 1887; University of the City of New York Medical Department, 1889; aged 85; died, Dec. 7, 1941, of cerebral hemorrhage and arteriosclerosis.

Wallace Kasson Harrison ✠ Chicago; Bennett Medical College, Chicago, 1877; College of Physicians and Surgeons of Chicago, 1884; an Affiliate Fellow of the American Medical Association; aged 93; died, Dec. 7, 1941.

Jesse Bird, Oklahoma City; University of Louisville (Ky.) Medical Department, 1896; member of the Oklahoma State Medical Association; aged 66; on the staff of the Samaritan Hospital, where he died, Dec. 9, 1941.

S. Dwight Stevenson, Columbus, Ohio; Medical College of Ohio, Cincinnati, 1890; member of the Ohio State Medical Association; aged 75; died, Nov. 26, 1941, in the White Cross Hospital following an appendectomy.

Warren Alexander Harper, Zapata, Texas; University of Tennessee Medical Department, Nashville, 1892; formerly acting assistant surgeon, United States Public Health Service; aged 75; died, Nov. 29, 1941, in Austin.

Ezra Eugene Osburn, Broughton, Ill.; St. Louis College of Physicians and Surgeons, 1904; aged 59; died, Dec. 1, 1941, in the Ferrell Hospital, El Dorado, of pneumonia and of injuries received in an automobile accident.

J. Michaux Corpening, Harrington, Wash.; University of Nashville (Tenn.) Medical Department, 1898; member of the Washington State Medical Association; aged 74; died, Nov. 1, 1941, of coronary thrombosis.

Winsor W. Warriner, Antioch, Ill.; Northwestern University Medical School, Chicago, 1902; aged 67; died, Nov. 30, 1941, in the Victory Memorial Hospital, Waukegan, of peritonitis and acute appendicitis.

Thomas Chason ✠ Donalsonville, Ga.; Vanderbilt University School of Medicine, Nashville, Tenn., 1892; at one time medical director and superintendent of Chason's Hospital; aged 68; died in November 1941.

Chalmer Middleton Harger, Seattle; University of Colorado School of Medicine, Denver, 1921; member of the Washington State Medical Association; aged 50; died, Nov. 13, 1941, of coronary thrombosis.

Helen P. Beattie Tennies, Green Bay, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 60; died, Oct. 30, 1941, of chronic myocarditis.

Leo John Nicola ✠ Chicago; Chicago Medical School, 1926; aged 41; on the staff of St. Francis Hospital, Evanston, Ill., where he died, Nov. 8, 1941, of patent foramen ovale and cirrhosis of the liver.

Clarence La Motte Boston, Noxen, Pa.; University of the City of New York Medical Department, 1884; member of the Medical Society of the State of Pennsylvania; aged 82; died, Dec. 1, 1941.

John A. Walker, Du Pont, Wash.; Northwestern University Medical School, Chicago, 1893; member of the Washington State Medical Association; aged 72; died, Nov. 15, 1941, in Phoenix, Ariz.

Benjamin Franklin Boyer, Riegelsville, Pa.; Long Island College Hospital, Brooklyn, 1867; Bellevue Hospital Medical College, New York, 1868; Civil War veteran; aged 99; died, Dec. 11, 1941.

Edgar Allen Cowles, Detroit Township, Minn.; University of Tennessee Medical Department, Nashville, 1892 and 1893; also a dentist; aged 80; died, Sept. 1, 1941, of hypertensive heart disease.

John Ellsworth Suter, Piedmont, W. Va.; College of Physicians and Surgeons, Baltimore, 1893; formerly mayor; bank president; aged 71; died, Nov. 29, 1941, of chronic myocarditis.

Harry Francis Rubel, Des Moines, Iowa; College of Physicians and Surgeons, School of Medicine of the University of Illinois, Chicago, 1904; aged 63; died, Nov. 25, 1941, of cirrhosis of the liver.

James Blaine Padgham, Ocheyedan, Iowa; State University of Iowa College of Medicine, Iowa City, 1909; member of the Iowa State Medical Society; aged 58; died, Nov. 9, 1941, of uremia.

Leon Knight Harding, Hopkinsville, Ky.; University of Tennessee Medical Department, Nashville, 1900; also a minister; aged 69; died, Nov. 29, 1941, in a hospital at Atlanta, Ga.

Walter Wynn Barnett, Fort Wayne, Ind.; Fort Wayne College of Medicine, 1886; veteran of the Spanish-American War; formerly county coroner; aged 84; died, Dec. 1, 1941.

James Lowry McBride ✠ Zanesville, Ind.; Medical College of Indiana, Indianapolis, 1892; served during the World War; aged 76; died, Nov. 29, 1941, of coronary thrombosis.

Joseph H. Satterthwaite, Trenton, N. J.; Hahnemann Medical College of Philadelphia, 1883; died, Nov. 23, 1941, in the William McKinley Memorial Hospital of heart disease.

John William Long, Sallis, Miss.; Kentucky School of Medicine, Louisville, 1908; member of the Mississippi State Medical Association; aged 56; died in November 1941.

James Malvern Halsey, Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1937; aged 30; was found dead, Nov. 23, 1941, of a bullet wound.

William Edward McDougal, Savannah, Tenn.; Vanderbilt University School of Medicine, Nashville, 1877; aged 87; died, November 19, at Memphis of cerebral hemorrhage.

George Brannan Allen ✠ South Bend, Ind.; Northwestern University Medical School, Chicago, 1916; aged 53; died, Dec. 4, 1941, of angina pectoris and coronary sclerosis.

Arminius Neulaender, Brooklyn; Magyar Királyi Pázmány Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1898; aged 67; died, Nov. 21, 1941.

Spurgeon Floyd Priestley, Stockton, Calif.; Barnes Medican College, St. Louis, 1898; member of the California Medical Association; aged 73; died, Nov. 23, 1941.

Paul Clifton Alexander, Redwood City, Calif.; Cooper Medical College, San Francisco, 1900; aged 67; died, Dec. 6, 1941, in the Palo Alto (Calif.) Hospital.

Oscar Leonard Spencer, Fiskeville, R. I.; Boston University School of Medicine, 1911; aged 75; died, Nov. 27, 1941, at Cranston of cardiorenal disease.

Frank H. Sidwell, Baltimore; University of Maryland School of Medicine, Baltimore, 1880; died, Nov. 22, 1941, in the Maryland General Hospital.

William Hubert Arrants, Sweetwater, Tenn.; University of Nashville (Tenn.) Medical Department, 1910; aged 59; died, Dec. 13, 1941, of myocarditis.

Erasmus Lear Reigle, Bloomsbury, N. J.; Jefferson Medical College of Philadelphia, 1889; aged 78; died, Nov. 29, 1941, in Easton, Pa., of empyema.

Esca D. Pope ✠ Hillister, Texas; Kentucky School of Medicine, Louisville, 1897; aged 69; died, Nov. 26, 1941, of cerebral hemorrhage.

James Sidney Smith, Greenville, Texas (licensed in Texas under the Act of 1907); aged 86; died in November in a hospital at Dallas.

Ernest Bartine Smith, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1900; aged 65; died, Nov. 28, 1941.

Frank C. Houser, Lincoln, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1887; aged 83; died, Nov. 26, 1941.

Amelia Landis Hess, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1892; aged 83; died, Nov. 25, 1941.

Guy Edward Beard, Algonquin, Ill.; Northwestern University Medical School, Chicago, 1910; aged 61; died, Dec. 11, 1941.

William Henry Kensinger, Miami, Fla.; Jefferson Medical College of Philadelphia, 1889; aged 85; died, Nov. 23, 1941.

Julius Purcell Haynes, Toledo, Ohio; Dartmouth Medical School, Hanover, N. H., 1888; aged 75; died, Nov. 17, 1941.

James Alexander Morrow, Philadelphia; Baltimore University School of Medicine, 1889; aged 81; died, Nov. 28, 1941.

Fred William Watt, Bieber, Calif.; Cooper Medical College, San Francisco, 1901; aged 66; died in November 1941.

Archie Wilson Barker, Springfield, Ill.; Barnes Medical College, St. Louis, 1899; aged 74; died, Dec. 4, 1941.

Haller Francis Keables, Burbank, Calif.; Rush Medical College, Chicago, 1890; aged 76; died, Nov. 2, 1941.

Esther Mitchell, Mount Sterling, Ky.; Rush Medical College, Chicago, 1903; aged 75; died, Nov. 30, 1941.

William K. Yorks, Chicago; Hering Medical College, Chicago, 1900; aged 76; died, Nov. 26, 1941.

Frederick Dow Lyon, Boston; Harvard Medical School, Boston, 1896; aged 72; died, Nov. 27, 1941.

Bureau of Investigation

CEASE AND DESIST ORDERS

Abstracts of Certain Federal Trade Commission Releases

The work of the Federal Trade Commission, in helping to protect the public against misrepresentation or fraud in the medical as well as other fields, has been greatly extended by the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act. The Food, Drug and Cosmetic Act of 1938 added to the Food and Drug Administration's control of the advertising claims and statements made on the labels of medicines or on the carton or in the accompanying leaflet, whereas what might be termed collateral advertising, that which appears in circulars, newspapers and magazines and over the air, comes more actively under the purview of the Federal Trade Commission, by virtue of the Wheeler-Lea Amendment.

THE JOURNAL has at various times commented on the activities of the Federal Trade Commission in this connection, even before the Wheeler-Lea Amendment gave it its added rights. In some cases the Commission may accept from the person or concern involved a stipulation that the objectionable practices or claims cited will be discontinued. In other cases the Commission issues what is known as a Cease and Desist Order, in which the individual, manufacturer or distributor cited is ordered to cease and desist from practices which have been declared objectionable.

Abstracts of some of the orders issued in 1941 follow:

Alcoban.—This was exploited as a treatment for alcoholism by Edwin L. Leisenring, trading as U. S. Drug and Sales Company, U. S. Drug Laboratories and U. S. Drug Company and Gordon Leisenring, both of Denver. The Federal Trade Commission ordered these individuals in January 1941 to cease representing that the product is a safe and competent treatment for alcoholism or that it removes the desire for alcoholic stimulants. They also were to discontinue any advertisements which fail to reveal that the use of Alcoban may result in serious injury to the nerves, tissues and lungs and may produce toxic conditions in the body.

Bowe's Tablets.—The advertising of this nostrum by R. G. Bowe and W. W. Hartman, trading as Bowe & Hartman, Toledo, Ohio, represented that some twenty ailments, including ulcers of the stomach, duodenum and intestine are due to or persist solely because of hyperacidity or the presence of excess acid in the body and that the Bowe product is a cure or remedy for hyperacidity and consequently for the ailments mentioned. In January 1941 the Federal Trade Commission ordered the promoters of Bowe's Tablets to discontinue making these misrepresentations and setting themselves forth as manufacturing pharmacists or as making the preparation that they sell.

Eucozone.—This was put out by Eucozone Laboratories, Inc., and by its successor, Universal Eucozone of America, Inc., Detroit. In March 1941 the Federal Trade Commission ordered the last-named concern to cease representing that the product is a germicide or has any therapeutic action beyond that of a mild antiseptic and counterirritant; that it is an internal antiseptic or will supply oxygen to the bloodstream; that it is of any value in treating colds, catarrh, sinus infection, rose fever, hay fever or localized congestions associated with such conditions, except that afforded by a mild antiseptic and counterirritant; that it is a cure or remedy for athlete's foot or has any action thereon, except as a mild antiseptic; that it is of any use in treating itch, carbuncles, irritations of the skin or hemorrhoids or is nonpoisonous or nonirritating and suitable or safe for internal use or that it is an ozonide of eucalyptol or has any therapeutic properties other than those of ordinary oil of eucalyptus or eucalyptol.

George's Compound.—J. Lawrence Walker and T. Kyle Woodward, trading as Walker and Woodward, and Nick A. George and John G. Brown, all of Casper, Wyo., promoted this product as having value in the treatment of all ailments except cancer and diabetes. Since the Federal Trade Commission's findings showed that the stuff was useless for the long list of disorders named, except as a temporary palliative, the defendants were ordered in February 1941 to cease and desist from making misrepresentations in their advertising. Incidentally, in at least 2 cases on record, George's Compound has been declared to violate the Pure Food and Drugs Act because of false claims made in or on the trade package. The first case was abstracted in this department of THE JOURNAL Dec. 23, 1939, page 2339.

Kongolene.—In January 1941 the Federal Trade Commission ordered the Kongo Chemical Company, Inc., of New York to discontinue certain misrepresentations in its advertising of this hair preparation. Among these were that the product is harmless to use, is a "purely vegetable product," will permanently straighten the hair or contribute to such straightening in any way other than by softening the hair temporarily, will promote the growth of the hair and prevent its falling out, will cure dandruff, will benefit the offspring of the user and is "the greatest discovery of the age." The concern also was ordered to discontinue any advertisements which failed to reveal that the use of the stuff might result in severe caustic action on the skin and scalp, with resulting burns. In April 1941 the Commission added to the order the proviso that the advertising of Kongolene need contain only a statement that the product should be used only as directed on the label, when such label contains a warning that the preparation might have a caustic action on the skin and scalp with resulting burns, and certain directions for the safe and proper use of Kongolene which were detailed in the original order.

Nu-Mode Products.—These are promoted by Harry S. Benham of Chicago, who has operated under such names as the Zone Company, Active Merchandisers, Active Medicine, Nu-Mode Company and American Medicine Company. In January 1941 the Federal Trade Commission ordered Benham to discontinue advertisements containing certain misrepresentations. Among these were that "Nu-Mode Vaginal Jelly" (also known as "A. M. Vaginal Jelly"), "Nu-Mode Hygiene Tablets," "Vaginal Suppositories and Douche Tablets," and "Speed Nu-Mode Hygiene Douche Tablets" constitute safe and effective preventives of conception or are a guaranteed method of preventing pregnancy; that "Nu-Mode Ladies Womb Supporter" is comfortable, efficient or sanitary or has therapeutic value; that "Athlete's Foot Salve" is a cure or remedy for athlete's foot or has value in its treatment in excess of temporarily relieving symptoms of itching and in some cases destroying superficial fungi; that "A. M. Wonder Salve" is a cure or remedy for eczema or other forms of itch or rash or has value in their treatment in excess of affording temporary relief from symptoms of itching, or that it has any properties effective in preventing infection or in treating ulcers, old sores, leg sores, acne or pimples.

Nuga-Tone.—National Proprietaries, Inc., of Chicago were ordered by the Federal Trade Commission in January 1941 to discontinue advertisements which represent Nuga-Tone as possessing any value in the treatment of nervous disorders or which fail to reveal that the use of the nostrum may result in chronic poisoning, irritation of the kidneys, nervous irritability, neuritis or some other conditions. In November 1937 the Commission likewise had ordered the National Laboratory of Chicago (which was then putting out Nuga-Tone) to discontinue certain false representations about the product, such as that it was an effective remedy for various stomach complaints and could be taken over long periods by any one without harmful results. The Commission also ordered the concern to cease representing itself as a "Laboratory," which may have been the reason that the firm name was changed. A lengthy discussion of Nuga-Tone and of the 2 year old child who had convulsions after swallowing some of the tablets appeared in THE JOURNAL May 17, 1924, page 1628.

Purex.—This product is put out as a germicide by the Purex Corporation, Ltd., Southgate, Calif., which in January 1941 was ordered by the Federal Trade Commission to withdraw from its advertising the misrepresentations that a solution containing any amount of less than 10 per cent of Purex is a competent or effective germicide for treating surface cuts or sores, or that a solution containing 2 tablespoons of Purex to each gallon of water is capable of killing all forms of bacterial life.

ReVigator Products.—In February 1941 the Federal Trade Commission ordered the ReVigator Corporation of Cleveland and its president, E. O. Loeber, to cease making certain misrepresentations in the sale of these. Among them were that the "ReVigator System of Home Treatment for the Scalp and Hair" provides a cure for falling, fading and thinning hair, dandruff and baldness. The Commission's findings were that the use of the "ReVigator Pressure Cap" alone or in combination with the other products in the treatment ("ReVigator Liquid Home Treatment for Scalp and Hair" and "ReVigator Liquid Shampoo") would not accomplish the results claimed and would have no therapeutic value in treating such conditions in excess of cleansing the hair and scalp and temporarily removing accumulated dandruff scales.

Texas Wonder.—For years this product has been represented as a cure for bladder and kidney disorders and has been the subject of actions by the Food and Drug Administration in more than one hundred instances over a period of years, on the charge that the label claims violated the Pure Food and Drugs Act. The first case was abstracted in this department of THE JOURNAL Feb. 22, 1919, page 591. In May 1932 the Federal Trade Commission dismissed a complaint against E. B. Hall and E. W. Hall of St. Louis on the charge of misrepresentations in advertising, at which time the Halls signed a stipulation agreeing to cease and desist from the practices charged. In February 1941 the Commission again was obliged to take action against the Halls and definitely ordered them to discontinue advertising that "Texas Wonder" is of value in the treatment of any of the ailments mentioned (kidney disorders, diabetes, rheumatism, swollen joints, weak or lame back, pains in the back or lumbago) except for such slight symptomatic relief as it may give in cases of swollen joints or pains in the back, because of its mild diuretic properties.

Vendol.—In January 1941 one David H. Fulton, trading as Vendol Company, Baltimore, was ordered by the Federal Trade Commission to eliminate from his advertising certain representations that the Commission declared to be false and misleading, such as that the product is a cure or remedy for constipation, stomach disorders, liver ailments, skin troubles or dyspepsia or is effective therefor, within certain limits; or, without making certain reservations, that the product will cure rheumatism, headaches, excess acidity, palpitation and some other things. In March 1937 David H. Fulton had promised the Commission that he would discontinue certain other misrepresentations in his advertising, such as that Vendol would correct any physical ailment including certain disorders of the stomach, liver and kidneys and that Vendol was prescribed by a physician.

X-Bazin.—This hair remover was represented by Hall & Ruckel, Inc., Brooklyn, as being noncaustic and in all cases entirely harmless. It was claimed that it discouraged the growth or delayed the appearance of hair for a substantial period of time, permanently eradicating hair, producing results essentially different from those obtained by the use of other depilatories and having the endorsement of scientists or physicians. In January 1941 the Federal Trade Commission ordered the concern to discontinue these misrepresentations.

SOME MISCELLANEOUS MEDICAL FRAUDS

A Variety of Schemes Debarred from the Mails

Fraud orders issued by the Post Office Department have frequently been the subject of extensive articles by the Bureau of Investigation in these pages of THE JOURNAL. Following are brief abstracts of some Fraud Orders not dealt with previously:

Bartlett "Cures" for Liquor and Tobacco Habits.—These were exploited from Birmingham, England, by a William Bartlett, who also used a Winnipeg, Canada, address and operated under various names including W. Bartlett Co. and Reliance Products. His "Bartlett Tobacco Treatment" was found to consist of gentian root to be chewed and some tablets to be swallowed, each containing more than 2 grains (0.13 Gm.) of quinine sulfate. Those who ordered the "Bartlett Liquor Remedy" received a prescription calling for 90 parts of sodium bicarbonate, 5 parts of powdered cuminum cyminum and 5 parts of powdered cinnamon, to be made up into 150 capsules of 1½ grains (0.1 Gm.) each. Medical experts testified that the most important factors in overcoming the liquor and tobacco habits are the determination and cooperation of the victim and that, since these cannot be supplied by drugs, no mixture could of itself cure either habit. A fraud order debarring the Bartlett nostrums from the mails was issued on July 30, 1940.

Blanchard's Lotion.—This was a curious combination of medical and religious quackery promoted by a Joseph Blanchard, who conducted his mail order scheme from Chicago, New York and Long Beach, Calif. He put out something variously called "Joseph Blanchard's Eczema Lotion" and "Trinity Lotion," which he represented as a cure for eczema, psoriasis, acne, leg ulcers and all infections and irritations of the ear, nose and mouth. With it went some circulars, one known as "Spiritual Copy No. 3," which exhorted in part: "Always apply Trinity Lotion for a Spiritual Soul Blessing . . ." Apparently discounting the alleged spiritual value in favor of the material one, the government chemists analyzed the product and reported it to be a slightly acidic, hydroalcoholic, mucilaginous liquid containing 0.04 per cent of mercury, 9.1 per cent of alcohol and an unidentified mixture of gums. As this combination would not cure such comparatively intractable conditions as psoriasis and eczema, the Post Office Department declared the thing a fraud and debarred it from the mails on August 31, 1940. In April 1935 a consignment of "Prof. Joseph Blanchard's Eczema Lotion" from Chicago was declared in a district federal court to be fraudulently represented on the label as an effective treatment for various forms of eczema, psoriasis, ulcers and some other cutaneous disorders. Government chemists reported that it consisted essentially of mercury bichloride, alcohol and water, with small amounts of borax and gum.

"Dr." O. T. Manson.—This Waycross (Ga.) Negro charlatan also worked the "numbers" game and sold advice and medicines chiefly among Negro victims. After promising an inquirer to "bring you strong and alive" for $3 and receiving that sum, he demanded an equal amount in addition to "fix up" the patient. When the second remittance of $3 was sent, Manson demanded an additional $2 and, on getting it, sent the customer an assortment of capsules and pills. The composition of both was found to be essentially calomel, aloin and podophyllin. As these are only common laxatives and would not "fix up" certain serious diseases whose symptoms were suggested by the customer, Manson's scheme was declared fraudulent and was debarred from the mails on June 7, 1940.

"Rev. Doc. J. H. Thompkins."—This self-styled "spiritualist and divine healer," as well as "world's greatest fortune teller," a Negro, operated first from Columbus, Ga., and later from Phenix City, Ala., selling "lucky hands." These, he claimed, would "Uncross Your Luck; Do Anything You Want Done; Cure Anything You Want Cured; Bring Back Husband; Wife or Friend; and Make You See Wonders; I See All, Tell All, Make All, Know All, Do All." A "lucky hand," for which Thompkins charged from $15 to $985, consisted chiefly of "science" of numbers, "religious" literature and a small bag of grayish white powder. Analysis showed this to consist of iron ore, powdered sulfur, ground capsicum, gentian and sage leaves. The customer was told to add a teaspoonful of urine to this daily for three days, "dress" it with perfume and wear it close to the body. As this mixture obviously would not cure anything, a Post Office fraud order was issued against Thompkins on Feb. 29, 1940.

Young and Smit.—This New York firm, which designated itself as an importer of medicines originating in the Dutch East Indies, consisted of a Ralph Young and an Antoinette Smit, who sold a long list of nostrums by mail. The chief one seems to have been "Herb Preparation No. 17," which a government analysis showed was a mixture of ground mint leaves, spurge, celery root and a species of bean. It was to be brewed and taken for rheumatism four times a day "until pains disappear." If one was "looking for a pleasant way to help take off excess fat," he was told that "'Bali Tea No. 15' is the answer to your prayer!" It was reported to consist chiefly of ground leaves and roots of mint, black elder and ginger. For disorders of the kidney and bladder there was "Koemis Koetjing No. 21," which was principally ground mint leaves. For liver troubles the concern sold "Hepatic Tea No. 2," a mixture of ground leaves and roots of herbs known as graptophyllum, hydrocotyle, curcuma, plantago major and blumea balsamifera. For "piles and rectal disturbances" there was "Herbal Preparation No. 9," a mixture of meibomia, acanthaceae, tamarindus, rhubarb and licorice roots and hydrocotyle centella, with traces of arbus and euphorbia. With it came "Java Lax Herbs No. 7," said to be composed of herbs having irritant laxative qualities. As expert medical testimony showed that none of these nostrums would produce the results claimed for them, a fraud order was issued against their promoters on Dec. 5, 1940.

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

The following items are abstracts of stipulations in which promoters of "patent medicines," cosmetics or medical devices have cooperated with the Federal Trade Commission to the extent of agreeing to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products.

Massagic.—This is the brand name for a line of shoes sold by the Weyenberg Shoe Manufacturing Company of Milwaukee, which represented that they would massage and exercise the feet and produce "massaging resilience," cause calluses to vanish and keep the feet "young." In a stipulation signed with the Federal Trade Commission in June 1941 the concern agreed to discontinue these misrepresentations.

Wa-Hoo Bitters.—This is put out by a Charles K. Wilson, trading as Old Indian Medicine Company and as Wa-Hoo Medicine Company, Toledo, Ohio. In January 1941 Wilson promised the Federal Trade Commission to cease representing that his product is a tonic or effective treatment for ailments of the blood, nerves, stomach, liver or kidneys or a remedy for rheumatism, gastritis and some other things, or that his "Old Indian Remedy" or "Old Indian Root and Herb Tonic" originated with the Indians before they were acquainted with recognized medical science. In 1916 and 1935 specimens of "Wa-Hoo Bitters" were declared in government courts to violate the Pure Food and Drugs Act because of false and fraudulent claims on the labels. Government chemists reported that analyses of specimens showed them to be aqueous solutions of epsom salt and salicylic acid, with indications of sassafras, gentian and prickly ash.

Valeria's Hair Grower.—That this will cause the natural oils of the scalp to be retained or overcome dryness of the scalp, stop excessive dandruff or falling hair or cause hair to grow constitutes advertising misrepresentations which Dave Boston and Willma Boston, trading as Valeria's Products and as Valeria's, Detroit, promised the Federal Trade Commission that they would discontinue in a stipulation that they signed in June 1941.

"Vegetrate" Products.—These are put out by Vegetrates, Inc., of Los Angeles and include "Vege-broth," "Vegetrate BF-1," "Vegetrate Formula No. CC-413" and thirteen other preparations. In February 1941 Vegetrates, Inc., stipulated with the Federal Trade Commission that it would cease representing that modern conditions cannot assure the full measure of life-sustaining organic minerals in the food one buys or cooks today; that the "Vegetrate" formulas are concentrated or contain all the concentrated goodness of nature's own vegetables or of vegetables grown in a specially mineralized soil, or that they give added protection to persons having low resistance. The concern also agreed to cease advertising that "Vegetrate 'Caroa' Fortified with Vitamin 'A'" is a protection against infection or that "Wheat Germ Oil Perles, Standard Potency Vitamin 'E'" are essential during pregnancy and are of the highest available potency and to discontinue various similar misrepresentations about others of its products. In April 1937 a district federal court had declared that certain of the Vegetrate products were fraudulently represented to be "health builders" and to cure various disorders. These included "BF-1," "Formula H. F. C. No. A-45" (for arthritis), "Formula H. F. C. No. D-44" (for diabetes), "Formula H. F. C. No. A-417" (for hay fever and asthma) and "Formula H. F. C. No. H-410" (for high blood pressure).

Williams Foot Preparations.—In January 1941 the Federal Trade Commission reported that William Newman, trading as Newman Products Company and The Newman Institute, Brooklyn, had promised to cease representing that his "Williams KornX," "Williams Foot Balm," "Williams Foot Shampoo' and "Williams Foot Powder" are competent remedies for athlete's foot, swollen ankles, ingrown toe nails, corns, warts and other foot troubles or that the use of these products would alleviate headaches, backaches or fatigue.

Z'Out.—This product, also known as "Dr. Frohlich's Z'Out Hair Destroyer," has back of it a Louis B. Frohlich, trading as the Frohlich Laboratories, and a David F. Griff, doing business as Frohlich Distributing Company, all of Seattle. In April 1941 they promised the Federal Trade Commission to cease representing that the product will permanently destroy hair, prevent the regrowth of hair or bring about the permanent removal of hair; that it possesses any marvelous qualities or that its development is the result of seven years' work or of any amount of work, effort, experimentation or research greater than that actually used or performed in its development. In recent years the Frohlich concern has sent out a report, attributed to a Seattle chemical laboratory, to the effect that the powder form of "Z'Out" seems to depend, for its action, on strontium sulfide.

Fairystone.—Ray G. Maloney, trading as Fairystone Manufacturing Company, and Willard J. Dungan and Arthur E. Maloney, doing business as Fairystone Distributing Company, all of Detroit, promised the Federal Trade Commission in April 1941 to cease representing that "Fairystone": is an "absolute sunburn protection" which filters out the burning or ultraviolet rays of the sun and permits other sun rays to gain access to the skin or that it will effectively conceal scars, birth marks or other cutaneous blemishes, or cause those who use it to look years younger, or will prove a competent remedy for pimpled or blotched skin.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 16-17, 1942. Council on Medical Education and Hospitals, Sec., Dr. William D. Cutter, 535 North Dearborn Street, Chicago.

MEDICAL CORPS, UNITED STATES NAVY

Examination. Assistant Surgeon with the permanent rank of Lieutenant (junior grade) and Acting Assistant Surgeon with the probationary rank of Lieutenant (junior grade), Jan. 5-9. Examination will be held at the Naval Hospitals at Chelsea, Mass., Newport, R. I., Brooklyn, Philadelphia, Norfolk, Va., Charleston, S. C., Pensacola, Fla., Corpus Christi, Tex., San Diego and Mare Island, Calif., Puget Sound, Wash., Great Lakes, Ill., Pearl Harbor, T. H., and Naval Medical Center, Washington, D. C. Apply Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, January 3, page 76.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Feb. 9-11. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* April in advance of the meeting of the American College of Physicians and June, in advance of the meeting of the American Medical Association. Applications should be on file 6 weeks in advance of the date of oral examination. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: New York, June. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral. Part II. Groups A and B* Atlantic City, May or June. Final date for filing application is March 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral and Written. All Groups.* Philadelphia, June, preceding the meeting of the American Medical Association. Final date for filing application is March 1. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PATHOLOGY: St. Louis, March 30-31. Final date for filing application is Jan. 30. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Cleveland, May 13, preceding the Region III meeting of the American Academy of Pediatrics. *Written.* Locally, February 14. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF RADIOLOGY: *Oral. All Groups.* Atlantic City, June 4. Final date for filing application is April 1. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written. Part I.* Various centers, March 2. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

District of Columbia Reciprocity Report

The District of Columbia Commission on Licensure reports 27 physicians licensed to practice medicine by reciprocity from June 10 through September 19. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of California Medical School		(1937)	California
University of Southern California School of Medicine		(1938)	California
George Washington University School of Medicine		(1931) (1937)	California, Pennsylvania
Georgetown University School of Medicine		(1937)	New Jersey
Howard University College of Medicine		(1937)	Virginia
Indiana University School of Medicine		(1936)	Indiana
Louisville Medical College		(1906)	Mississippi
University of Louisville Medical Department		(1910)	Texas
University of Maryland School of Medicine and College of Physicians and Surgeons		(1937), (1939)	Maryland
Detroit College of Medicine and Surgery		(1933)	Michigan
Columbia University College of Physicians and Surgeons		(1927)	New York
Cornell University Medical College		(1937)	New York
Long Island College of Medicine		(1938)	Penna.
New York University College of Medicine		(1936)	New York
University of Cincinnati College of Medicine		(1933)	Ohio
Hahnemann Medical College and Hospital of Philadelphia		(1937), (1938)	Penna.
Jefferson Medical College of Philadelphia		(1938)	Penna.
Temple University School of Medicine		(1938)	Penna.
Medical College of the State of South Carolina		(1935)	S. Carolina
Meharry Medical College		(1939)	Tennessee
University of Tennessee College of Medicine		(1921)	Arkansas
Vanderbilt University School of Medicine		(1915)	Tennessee
University of St. Andrews Conjoint Medical School		(1936)	New York
Osteopath *			Michigan

* Licensed to practice surgery.

Oregon October Report

The Oregon State Board of Medical Examiners reports 10 physicians licensed to practice medicine by reciprocity and 1 physician so licensed on endorsement of credentials of the National Board of Medical Examiners from September 20 through October 16. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Stanford University School of Medicine		(1939)	California
University of Colorado School of Medicine		(1939)	Colorado
Northwestern University Medical School		(1924)	Nebraska
University of Louisville School of Medicine		(1940)	Kentucky
St. Louis University School of Medicine		(1925) (1939)	Nevada, Missouri
New York Homeopathic Medical College and Flower Hospital		(1935)	New York
University of Oklahoma School of Medicine		(1937)	Kansas
University of Oregon Medical School		(1940)	California
Osteopath *			Nebraska

School	LICENSED BY ENDORSEMENT	Year Grad.
Johns Hopkins University School of Medicine		(1934)

* Licensed to practice surgery.

South Carolina November Report

The State Board of Medical Examiners of South Carolina reports the oral and written examination for medical licensure held at Columbia, Nov. 10-11, 1941. The examination covered 17 subjects and included 39 questions. An average of 75 per cent was required to pass. Three candidates were examined, all of whom passed. Nine physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
University of Louisville School of Medicine		(1937)	1
Medical College of the State of South Carolina		(1941, 2)	2

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Emory University School of Medicine		(1940)	Georgia
University of Louisville School of Medicine		(1939)	Kentucky
University of Maryland School of Medicine and College of Physicians and Surgeons		(1929)	Maryland
Meharry Medical College		(1929), (1940, 3)	Tennessee
University of Virginia Department of Medicine		(1936) (1937)	N. Carolina, Virginia

Wyoming October Report

The Wyoming State Board of Medical Examiners reports the written examination held at Cheyenne, Oct. 6, 1941. Five candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists		(1941)	1
Louisville Medical College		(1902)	1
University of Louisville School of Medicine		(1940)	1
University of Oklahoma School of Medicine		(1939)	1
University of Pennsylvania School of Medicine		(1938)	1

District of Columbia November Report

The District of Columbia Board of Examiners in Medicine and Osteopathy reports the written examination for medical licensure held in Washington, Nov. 10-12, 1941. The examination covered 9 subjects and included 60 questions. An average of 75 per cent was required to pass. Ten candidates were examined, all of whom passed. Twenty-one physicians were licensed to practice medicine on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
George Washington University School of Medicine		(1939), (1940, 3)	4
Georgetown University School of Medicine		(1938), (1939), (1940)	3
Howard University College of Medicine		(1940, 2)	2
Rush Medical College		(1922)	1

School	LICENSED BY ENDORSEMENT	Year Grad.
George Washington University School of Medicine		(1939, 2), (1940)
Georgetown University School of Medicine		(1937), (1938), (1939, 2), (1940, 7)
Rush Medical College		(1932)
Johns Hopkins University School of Medicine		(1933)
Harvard Medical School		(1937)
Tufts College Medical School		(1937)
Columbia University College of Physicians and Surgeons		(1928)
Duke University School of Medicine		(1939)
University of Oregon Medical School		(1929)

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Right of Board of Medical Examiners to Revoke License of Naturopath; Right of Naturopaths to Prescribe Drugs.—The plaintiff, Henry Gross, obtained a certificate issued by the board of examiners of the Association of Naturopaths of California and, on the purported authority of that certificate, commenced the practice of naturopathy in the city of Los Angeles. In 1909 a statute was enacted which provided that persons who held "an unrevoked certificate" issued by the Naturopathic Association and who had practiced naturopathy prior to the passage of the 1909 act were authorized to continue such practice and entitled to have such certificate endorsed by the board of medical examiners. This act also provided:

> But all certificates herein mentioned may be revoked for any unprofessional conduct, in the same manner and upon the same grounds as if they had been issued under this act.

In 1913 the existing medical practice act was repealed and a new one enacted under which persons desiring to practice naturopathy could secure drugless practitioners' certificates from the board of medical examiners. In 1937 the medical practice act was codified and became a part of the Business and Professions Code. Subsequently the plaintiff was charged with a violation of the Business and Professions Code in that he administered and prescribed drugs to his patients. The board of medical examiners found him guilty and placed him on probation for three years. Accordingly the plaintiff filed a petition for a writ of mandate directing the board to dismiss the charges which had been filed against him and restraining the board from preventing the plaintiff from prescribing for his patients. From a judgment sustaining the board's demurrer and dismissing the plaintiff's petition, the plaintiff appealed to the district court of appeal, second district, division 2, California.

The plaintiff first contended that the board of medical examiners had no jurisdiction over him because all of the statutory provisions relating to naturopaths were eliminated from the 1913 law creating the respondent board. The district court of appeal said that the legislature, by comprehensive enactments, intended to regulate all persons engaged in any of the various healing arts. When the plaintiff's certificate was endorsed pursuant to the provisions of the 1909 act, the effect was the same as if the board of medical examiners had actually issued a new license. Furthermore, the 1909 act specifically authorized disciplinary proceedings against the holders of such endorsed certificates. The court therefore held that the board had jurisdiction over the plaintiff and that it would be unreasonable to conclude that all practitioners of the healing art were subject to regulation except those who were practicing naturopathy in 1909.

The plaintiff also contended that he did not perform any acts not permitted by his naturopathic certificate. The laws of California did not define naturopathy but the articles of incorporation of the Association of Naturopaths provided that its members were authorized to treat patients by the use of "herbs" and other specifically named agencies. The evidence showed that, for at least one of his patients, the plaintiff prescribed a substance known as Alpha Naphco, which bore the following matter on its label, as read into the record by the Deputy Attorney General:

> Alpha Naphco, formerly Benetol. Activity—(spelling) Phen. coef.—I imagine that is "coefficient." (continuing reading): "—H. L. Test 1.46. Phenol coefficient against yellow pus germs in ½ blood serum ½ saliva at body heat 3.11. Inert Ingredient—Inred.—" It reads here—(continuing reading): "Glycerine 32%, Water 40%. Contents—Not less than six ounces liquid. Carel Laboratories, Redondo Beach, California, Formerly Benetol Products Co."

He also prescribed a beef extract which was not composed of herbs in their natural form. Expert testimony, said the court, was not needed to show that the prescription of capsules of grayish powder and a liquid with a large content of glycerin could not be classified as the use of herbs. The district court of appeal therefore held that the evidence was sufficient to sustain a finding that the defendant had prescribed substances which were a part of materia medica and could not be classified as "herbs." The action of the board was therefore sustained.—*Gross v. Molony, 102 P. (2d) 816 (Calif., 1940).*

Contracts: Validity of Agreements in Restraint of Professional Practice.—The plaintiff and the defendant formed a partnership for the practice of medicine in Lumberton, N. C. The agreement provided for the dissolution of the partnership on ninety days' written notice and contained a provision under which the defendant agreed not to engage in the practice of medicine in Lumberton, or within 100 miles thereof, for a period of five years following the dissolution of the partnership. Later the partnership was dissolved and thereafter the defendant opened an office in Lumberton for the practice of medicine. The plaintiff brought suit to enjoin the defendant from practicing medicine contrary to the partnership agreement and, from an order granting a restraining order and continuing it until final hearing, the defendant appealed to the Supreme Court of North Carolina.

The plaintiff contended that the contract was clear and unambiguous and freely entered into; the defendant contended that it was void because contrary to public policy. The Supreme Court said that, actually, public policy is concerned with both sides of the question; it favors the enforcement of contracts intended to protect legitimate interests and frowns on unreasonable restrictions. In the opinion of the court it is as much a matter of public concern to see that valid contracts are observed as it is to frustrate oppressive ones. The determinative factor is the reasonableness of the agreement. The Court found that both of the parties regarded the restriction as reasonable when they signed the agreement and that both were familiar with the situation. The defendant himself had insisted that an agreement be signed, and he did not then object to the restrictive covenant. Both parties felt, at the time the agreement was executed, that the plaintiff had a legitimate interest to protect, and the restriction itself was reasonably limited as to both time and place. The Supreme Court therefore held that the defendant was bound by his agreement and could not, looking at it retrospectively, regard it as unwise and seek to void it on grounds of public policy. The contract was not forbidden by any principle of policy or law. The defendant could be as useful to the public at any other town as he could at Lumberton, and the lives and health of persons in other villages were just as important. Communities therefore were not injured, concluded the Court, by a stipulation of this kind between two physicians. The restraining order was affirmed.—*Beam v. Rutledge, 9 S. E. (2d) 476 (N. C., 1940).*

Chiropractors: License as Prerequisite to Collection of Fees.—In this case the court of civil appeals of Texas denied relief to a chiropractor who had sued a patient to recover compensation for services rendered. The chiropractor had no license to practice in Texas and the court held that, since he had no legal right to perform the services, he could not lawfully make and collect a charge therefor.—*Park v. Coulson, 139 S. W. (2d) 667 (Texas, 1940).*

Society Proceedings

COMING MEETINGS

Annual Congress on Industrial Health, Chicago, Jan. 12-13. Dr. C. M. Peterson, 535 North Dearborn St., Chicago, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 16-17. Dr. William D. Cutter, 535 North Dearborn St., Chicago, Secretary.

American Academy of Orthopedic Surgeons, Atlantic City, N. J., Jan. 11-15. Dr. Rexford L. Diveley, 1103 Grand Ave., Kansas City, Mo., Secretary.

American Orthopsychiatric Association, Detroit, Feb. 19-21. Dr. Norvelle C. LaMar, 149 East 73d St., New York, Secretary.

Central Surgical Association, Chicago, Feb. 27-28. Dr. George M. Curtis, Ohio State University, Columbus, Ohio, Secretary.

Pacific Coast Surgical Association, San Francisco and Del Monte, Calif., Feb. 17-20. Dr. F. L. Reichert, Stanford University Hospital, San Francisco, Secretary.

Society of Surgeons of New Jersey, Trenton, Jan. 28. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1931 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

22:439-582 (Oct.) 1941

*Rheumatic Infection in Childhood: Influence of Type of Onset and Calendar Year of Onset. Rachel Ash, Philadelphia.—p. 439.
Further Observations on Mechanism of Production of Short PR Interval in Association with Prolongation of QRS Complex. C. C. Wolferth and F. C. Wood, Philadelphia.—p. 450.
*Arteriosclerotic Aneurysms and Senile Ectasia of Thoracic Aorta. M. deG. Ruffin, B. Castleman and P. D. White, Boston.—p. 458.
*Normal and Abnormal Esophageal Electrocardiogram, with Particular Reference to Myocardial Infarction. J. Nyboer, New York.—p. 469.
*Objective Evidence of Efficacy of Medicinal Therapy in Angina Pectoris. A. S. Freedberg, J. E. F. Riseman and E. D. Spiegl, Boston.—p. 494.
*Octyl Nitrite in Treatment of Angina Pectoris. A. S. Freedberg, E. D. Spiegl and J. E. F. Riseman, Boston.—p. 519.
Effect of Abrasion of Surface of Heart on Intercoronary Communications. E. J. Stanton, P. Schildt and C. S. Beck, Cleveland.—p. 529.
The Coronary Operation. C. S. Beck, Cleveland.—p. 539.
Sympathectomy and Experimental Occlusion of Coronary Artery. A. Yodice, Buenos Aires, Argentina.—p. 545.

Rheumatic Infection in Childhood.—Ash made a follow-up study of 583 children whose rheumatic infection had occurred during 1922 to 1936, inclusive, and who were cared for at the Children's Hospital. In 1939, 527, or 90.4 per cent, of these children were traced. Twenty-six of the untraced children had been followed previously for three to thirteen years; thus the average follow-up period for 553 rheumatic children was nine and six-tenths years. At the end of this time, 64.2 per cent had signs of valvular heart disease and 21.7 per cent had died of rheumatic infection. An additional 3.5 per cent had died of bacterial endocarditis or another associated infection. The prognosis of acute carditis was most grave and that of chorea most favorable. Children with a diagnosis of potential heart disease at the onset frequently tended to remain free of signs of heart disease. The severity of the rheumatic infection tended to decrease during the period of observation, especially among patients whose primary symptoms were arthritic. The improvement could not be ascribed to racial variation, changes in type of onset, progressive decline in recurrences or a modification in the admission policy of the hospital. It is undetermined whether the intensive supervision of the child from the first manifestation of the disease has had any effect on the natural trend to improvement. The recently adopted conservative attitude toward tonsillectomy has had no unfavorable influence. Transference to a convalescent home, although insuring stabilization of the infection, is no substitute for absolute bed rest for the child with any degree of active infection. Part, if not all, of the improvement would seem to be due to a spontaneous change in the character of the disease. In spite of the seeming decline in severity, rheumatic infection remains the most serious disease which attacks children past infancy.

Arteriosclerotic Aneurysms and Ectasia.—Ruffin and his co-workers were prompted by the death from internal hemorrhage, caused by rupture of the thoracic aorta, of 2 old women with nonsyphilitic thoracic aortic aneurysms to survey the literature and to analyze the postmortem records of the Massachusetts General Hospital. Their first case was one of arteriosclerotic aneurysm and the second one of dissecting aneurysm in an aorta which was the seat of senile ectasia. Of the 9,600 cases in which necropsy was performed at the hospital since 1897 aneurysm was observed in 116; 17 were cases of true dissecting aneurysm with medionecrosis aortae cystica, in 13 cases small "dissections" had occurred mostly in and about small atherosclerotic plaques and of the 86 remaining cases the aneurysms in 21 were in the ascending aorta, in 37 mainly in the arch, in 8 in the descending thoracic portions and in 20 in the abdominal aorta. Of the 66 cases of thoracic aneurysm, the disorder in 60 was syphilitic and in 3 arteriosclerotic, and in 3 there was considerable dilatation of the ascending aorta without arteriosclerosis—a condition that the authors term "senile ectasia." Of the 20 abdominal aortic aneurysms, 3 were syphilitic and 17 were arteriosclerotic; all of the former and 6 of the latter ruptured. The average age at death of the patients with syphilitic aneurysms was 46.4 years, and of those with arteriosclerotic aneurysms and senile ectasia it was 72.7 years. From the authors' cases it is to be realized that even large thoracic aortic aneurysms may be of an arteriosclerotic or senile nature and that they too may rupture, with fatal hemorrhage. Important clues to the diagnosis of an arteriosclerotic aneurysm and senile ectasia of the thoracic aorta, in some cases at least, are old age, female sex and a negative serologic reaction. The authors conclude that in the future, as a result of a constantly aging population and a gradual reduction of syphilis among the masses, these conditions will be found more often.

Esophageal Electrocardiogram and Myocardial Infarction.—Nyboer studied the standard lead, the selected precordial lead (4) and the selected esophageal lead from the ventricular and auricular levels of 4 normal subjects, of 1 patient with anterior myocardial infarction, of 10 with posterior myocardial infarction and of 10 with a history and/or physical signs suggestive of myocardial disease. The esophageal electrocardiogram from the ventricles was as specifically diagnostic of posterior myocardial infarction as the precordial electrocardiogram is diagnostic of infarction of the anterior wall. The criteria for a diagnosis of posterior myocardial infarction by the esophageal ventricular lead are essentially the same as those for a diagnosis of anterior myocardial infarction by the precordial lead.

Therapy in Angina Pectoris.—Freedberg and his collaborators determined the pharmacodynamic action of drugs on 15 patients with angina pectoris repeatedly mounting and descending a two step stairway. The administration of glyceryl trinitrate, theobromine with sodium acetate or quinidine sulfate enabled some patients to do a measurably greater amount of work under standardized conditions and, at the same time, prevented the changes in the ST segment which result from exercise. Inert drugs had no such effect. Digitalis was given to the patients and in some it increased the frequency of attacks in daily life, decreased the amount of work which could be performed under standardized conditions, increased the electrocardiographic changes following exertion and produced electrocardiographic changes similar to those observed after exercise without medication.

Treatment of Angina Pectoris.—According to Freedberg and his collaborators, the inhaling of octyl nitrite by patients with angina pectoris was effective in preventing attacks on exertion and in shortening the duration of such attacks. Its action is similar to that of glyceryl trinitrate and amyl nitrite. Inhalation of octyl nitrite permits more rapid absorption but makes accurate dosage impossible. The commercial inhalers now available are not satisfactory. Dose for dose, octyl nitrite is much more costly than glyceryl trinitrate but less so than amyl nitrite.

American Journal of Clinical Pathology, Baltimore

11:741-796 (Oct.) 1941

*Congenital Heart Disease as Cause of Sudden Unexpected Death in Children Under One Year of Age. S. A. Levinson, Chicago.—p. 741.
Unusual Cardiac Pathology. V. J. Dardinski, Washington, D. C.—p. 754.
Metastatic Melanoma with Lymphatic Leukemia Blood Picture. B. E. Konwaler, Pueblo, Colo.—p. 761.
Universal Blood and Hetero Group Transfusions. Anne M. Strauss and S. O. Levinson, Chicago.—p. 766.
Postvaccinal Meningoencephalomyelitis: Report of Case. T. M. Dunn and R. H. Rigdon, Memphis, Tenn.—p. 771.
*Factors in Mortality of Appendicitis. F. W. Mulsow, Cedar Rapids, Iowa.—p. 777.
Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christians Disease): Report of Case. C. P. Larson and B. N. Ootkin, Tacoma, Wash.—p. 781.

Congenital Heart Disease as Cause of Sudden Death.—According to Levinson, in the Cook County Hospital during the years 1929 through 1939 necropsy was performed on 12,837 infants, children and adults. There were 78 cases, or 0.607 per

cent, of congenital heart disease in children of 1 year or less. In 35 of the 78 cases the disease was diagnosed clinically, whereas in 43 there was no previous history or clinical evidence of congenital disease of the heart or of the blood vessels. Of 1,921 cases in which necropsy was done in the Research and Educational Hospitals from the years 1927 through 1939 there was gross and definite evidence of congenital heart disease in 23. Of 8,500 cases investigated by the author as coroner's physician during the last thirteen years, 50 per cent, or 4,250, were instances of sudden or unexpected death; that is, the persons died without having been previously ill or without having been under a physician's care. In this group there were 8 cases in which children less than 1 year of age had congenital defects of the heart or of the blood vessels directly responsible for the unexpected death. When questioned the parents of the 8 children stated that the children had not been sick at any previous time. Some of the children had been taken to the Infant Welfare Station, and their mothers had not been warned of any evidence of illness.

Factors in Appendicitis Mortality.—Mulsow studied 122 patients who died from appendicitis in Cedar Rapids during the last ten years. He found that the morbid anatomy of the appendix was the most important factor in the death of 41 of the 122. Only 12 of the 41 gave a history of taking laxatives; they were not in the extreme ages of life and they were seen within forty-eight hours by a surgeon. All but 5 were operated on. One of the 5 was treated by Christian science and 2 by chiropractic measures. At the necropsy of these 3 patients, a gangrenous ruptured appendix, with general peritonitis, was observed. The fourth of the 5 patients was a woman of 35 with a badly deformed spine and chest, in whom the diagnosis was uncertain during life, but at necropsy a ruptured appendix, with peritonitis, was observed. The fifth patient, a woman of 46 with rheumatic heart disease, was regarded as a poor surgical risk. Of the one hundred and twenty-two appendixes twenty-five were in the retrocecal position, thirty-nine had concretions in the lumen and one had a diverticulum. Seventeen, or about 13 per cent, of the deaths followed the removal of a noninflamed appendix. Six of the 17 deaths were due to peritonitis, 3 to pneumonia, 2 each to paralytic ileus and embolism and 1 each to anesthesia, septicemia, coronary occlusion and surgical shock. Concretions in the lumen or kinks in the appendix make acute appendicitis a dangerous disease. Concretions were found in three fourths of the perforated appendixes and in half of the gangrenous ones. Fourteen of the patients who died of a ruptured appendix had a history of a previous attack, and because of the previous recovery they delayed in calling a surgeon. Before the age of 15 there were twice as many deaths of girls as of boys, between 15 and 50 twice as many men as women died and after 50 the number of deaths was about equal for the two sexes.

American J. Digestive Diseases, Fort Wayne, Ind.

8:361-400 (Oct.) 1941

Some Recent Advances in Physiology of Alimentary Tract. A. C. Ivy, Chicago.—p. 361.
Enterogastrone—Significant Steps in Development of Present Conceptions. J. P. Quigley, Cleveland.—p. 363.
Present Status of Urogastrone. J. S. Gray, Chicago.—p. 365.
Gastric Secretory Depressant in Urine. M. H. F. Friedman and D. J. Sandweiss, Detroit.—p. 366.
*Effect of Urine Extracts on Peptic Ulcer: Experimental and Clinical Study. D. J. Sandweiss, M. H. Sugarman, M. H. F. Friedman, H. C. Saltzstein and A. A. Farbman, Detroit.—p. 371.
Qualitative Circulatory Deficiencies Observed in Peptic Ulcer: I. Chemical Composition of Blood. Helena E. Riggs, J. G. Reinhold, R. S. Boles and P. S. Shore, Philadelphia, with technical assistance of Charlotte S. Chornock and Florence Meshkov.—p. 383.
Comparison of Meulengracht and Sippy Therapies in Care of Bleeding Peptic Ulcers. E. S. Emery Jr., Boston.—p. 387.
Gastroscopic and Histologic Studies of Stomach with Gastric and Extragastric Disease During Life and at Autopsy. W. A. Swalm and L. M. Morrison, Philadelphia.—p. 391.

Effect of Urine Extracts on Peptic Ulcer.—Sandweiss and his collaborators point out that from 1 to 5 mg. of extract of pregnancy urine and normal female urine benefited experimental ulcers in Mann-Williamson dogs in the presence of an essentially unaltered gastric acid juice. The beneficial effect was due to the stimulation of fibroblastic and epithelial proliferation and the formation of new blood vessels. Urine contains a gastric secretory depressant. Therapy with the present available extract has shown encouraging results in 63 patients with chronic duodenal ulcer. Treatment did not prevent recurrences. While the number of relapses within six months and one year was approximately the same as obtained in similar patients treated with diet and alkalis, the patients treated with urine extract enjoyed a more liberal diet. While the patients treated with other parenteral products also enjoyed a more liberal diet, fewer of these patients became symptom free during treatment and more of them had relapses within six months and one year as compared with the patients treated with urine extract. It is probable that diet, alkalis and urine extract might produce even better results. In view of the encouraging experimental and clinical results the authors are carrying out further clinical studies with larger doses of a more highly concentrated urine extract.

Annals of Internal Medicine, Lancaster, Pa.

15:629-782 (Oct.) 1941

Mass Immunization Against Typhus Fever. R. E. Dyer, Bethesda, Md.—p. 629.
*Cerebral Embolism in Mitral Stenosis. A. W. Harris, Dallas, Texas, and S. A. Levine, Boston.—p. 637.
Pulmonary Infarction in Heart Disease. L. E. Hines and J. T. Hunt, Chicago.—p. 644.
Chemistry of Vitamin K. L. F. Fieser, Cambridge, Mass.—p. 648.
*State of Sensory and Motor Centers in Patients with Hypothyroidism. N. Enzer, E. Simonson and S. S. Blankstein, Milwaukee.—p. 659.
Concept of Psychosomatic Rheumatism. J. L. Halliday, Glasgow, Scotland.—p. 666.
Schizophrenia: Neurobiologic Approach. A. O. Hecker, Indianhead Gap, Pa.—p. 678.
*Plasma Creatinine Determination as Test of Low Grade Kidney Damage. A. Arkin, H. Popper and F. A. Goldberg, Chicago.—p. 700.
*Hunner Ulcer of Bladder (Review of 100 Cases). C. C. Higgins, Cleveland.—p. 708.
Roentgen Study of Cavities in Pulmonary Tuberculosis: Cavity Changes Under Collapse and Noncollapse Measures. R. C. Edson and A. L. Starkey, Hopemont, W. Va.—p. 716.
Idiopathic Cardiac Enlargement Occurring in Infants and Children. J. M. Neely, Lincoln, Neb.—p. 727.

Cerebral Embolism in Mitral Stenosis.—Harris and Levine tried to determine why a sudden cerebral embolism developed in 46 patients with mitral stenosis from the Peter Bent Brigham Hospital and 24 from private practice while they were in a fair state of cardiac compensation. Auricular fibrillation was present in 55 patients, and in only 3 of them was it transient. The average duration of the fibrillation was twenty-two months; the range was from three days to nine years. It appears that the cerebral accident is apt to occur during the early weeks or months after the onset of persistent auricular fibrillation. In 5 patients, after the fibrillating state reverted to a normal rhythm either spontaneously or after quinidine therapy embolism took place within a few hours or a day or two. In 17 with regular rhythm at the time of the cerebral accident fibrillation of the auricles, as far as could be ascertained, had not been present previously. The "immediate mortality" (24 deaths) and the survival period of those recovering from embolism were not influenced by auricular fibrillation, despite the fact that hypertension and congestive failure were more common in this group. There were 23 with and 49 without congestive heart failure; the "immediate mortality" for the former was 53 per cent, and for the latter it was 24 per cent. The 4 patients with congestive failure with regular rhythm died "immediately," while only 4 of 13 with regular rhythm but without failure died "immediately." It seems that cerebral embolism is more likely to occur in patients with mitral stenosis having little objective evidence of congestive heart failure than it is in those with advanced failure who are bedridden. It occurs more frequently in compensated than in decompensated mitral stenosis because the former state lasts longer.

Sensory and Motor Centers in Hypothyroidism.—Enzer and his associates determined the state of the sensory and motor centers of 13 patients with a decreased metabolic rate and hypothyroidism by the fusion frequency of flicker and finger movements. The sensory and the motor centers were deteriorated in these patients. In some patients the decrease of fusion frequency and in others the decrease of motor frequency was more pronounced. Eleven of 13 patients had values of fusion frequency lower than the lowest value of 45 normal control subjects; the other 2 had values that coincided with the lowest normal values. This explains the disposition to increased fatigability of such

patients, as the fusion frequency of flicker is diminished in nervous fatigue. Weakness of motor centers is shown by the decrease of frequency during performance.

Plasma Creatinine Determination.—According to Arkin and his colleagues, their new simple determination of plasma creatinine provides a diagnostic procedure for detecting mild disturbances of glomerular filtration and, consequently, of renal damage of low grade. These disturbances are of diagnostic and prognostic importance in acute nephritis, chronic nephritis, nephrosis, nephrosclerosis, urologic conditions and heart failure. In extrarenal azotemia the increase of the creatinine level is relatively less substantial than that of urea and nonprotein nitrogen, apparently because of an increased reabsorption of urea. The reagents are a saturated solution of picric acid and 10 per cent chemically pure sodium hydroxide. To 12 cc. of picric acid 4 cc. of oxalated plasma is added, drop by drop. The test tube is shaken and immersed in a boiling water bath for fifteen seconds. The mixture is filtered through a no. 44 Whatman filter. To 10 cc. of the cooled filtrate 0.5 cc. of sodium hydroxide is added and the mixture is again filtered. The colored solution formed is read with monochromatic light with a filter of 530 millimicrons twenty minutes after the sodium hydroxide has been added. The determination is made with a colorimeter, a photometer or a photoelectric colorimeter. By the aid of a known creatinine solution a comparison curve is made in the range between 0.5 and 3 mg. per hundred cubic centimeters of plasma. If the creatinine concentration exceeds this range the plasma is diluted with water. The normal level lies between 0.6 and 0.95 mg. per hundred cubic centimeters of plasma. It is constant in normal persons on different days or at different times of the day, even after the ingestion of food or fluid. Any slight increase over 1 mg. per hundred cubic centimeters is a probable sign of disturbed glomerular filtration. The method has been used four hundred and seventy-four times for 278 patients with renal disturbances or diseases commonly associated with extrarenal azotemia.

Hunner Ulcer of Bladder.—Higgins employed various types of therapy for his 100 patients with Hunner ulcer, but he observed that conservative treatment, fulguration of the ulcer and overdistention of the bladder, is the best method. Foci of infection must be eradicated. Of 69 patients receiving such treatment 17 were definitely cured, 10 were lost track of, 14 were not improved and 28 were improved. Four patients also had other operative procedures; 1 of them was cured and 1 was improved.

Archives of Ophthalmology, Chicago

26:727-944 (Nov.) 1941

Random Reminiscences of Last Century European Ophthalmologists. A. W. Stirling, Baldwin, Ga.—p. 727.
Change of Axis of Astigmatism on Accommodation. W. L. Hughes, Hempstead, N. Y.—p. 742.
Retinal Periphlebitis in Course of Acute Exudative Choroiditis. A. Knapp, New York.—p. 750.
*Lime Burns of Eye: Use of Rabbit Peritoneum to Prevent Severe Delayed Effects: Experimental Studies and Report of Case. A. L. Brown, Cincinnati.—p. 754.
Hydrogel Qualities of Vitreous. L. von Sallmann, New York.—p. 770.
Tumors of Conjunctiva and Lids: Brief Review. B. Samuels, New York.—p. 789.
*Causes of Blindness in Pennsylvania: Analysis of Blindness in Over 30,000 Eyes. A. Cowan and Bernice C. English, Philadelphia.—p. 797.
Modification of Brewster Stereoscope for Clinical Requirements. E. Krimsky, Brooklyn.—p. 808.
Ocular Conditions Associated with Coliform Bacteria: Clinical and Experimental Observations on Coliform Bacteria Infections of Upper Respiratory Tract. C. Berens and Edith L. Nilson, New York.—p. 816.
Retinal Phlebosclerosis. G. G. Gibson and L. W. Smith, Philadelphia.—p. 840.
Ophthalmic Zinc Sulfate Solutions: Buffered, Isotonic and Preserved. L. Arrigoni, L. Fischer, Seattle, and G. A. Tozer, Everett, Wash.—p. 852.
Tonometric Standardization: Method of Increasing Accuracy of Tonometry. D. O. Harrington and A. H. Parsons, San Francisco.—p. 859.
Ophthalmic Aspects of Acute Oxygen Deficiency. R. A. McFarland, Boston; J. N. Evans, Brooklyn, and M. H. Halperin, Boston.—p. 886.

Lime Burns of Eye.—Since the prognosis of severe burns of the eye treated conservatively (by irrigation and with atropine and ointment) has been bad, Brown used several membranes in experiments on rabbits to prevent the burned palpebral conjunctiva from being in constant contact with the corneal surface, which he found acted as a corrosive agent. He found rabbit peritoneum to be the tissue of choice. He cites 4 patients who sustained lime burns of the eye and in whom he used rabbit peritoneum to protect the surfaces of the eye from coming in contact with the burned palpebral conjunctiva. Affected surfaces must be completely separated by smooth tissue to allow healing. A section of peritoneum about 4.5 by 10 cm., passed through three successive washes of warm physiologic solution of sodium chloride, is used. The needles of two double armed no. 5 silk sutures are passed through the center area of the tissue about 2.5 cm. apart. The needles are then passed through the upper fornix, the tissue is placed as far as possible into the upper fornix and the sutures are then tied over buttons to prevent their cutting through the skin. The tissue is smoothed out over the eye and similarly sutured in the lower fornix. Any medication or irrigation may be applied beneath either surface of the flap. The flap is removed when the cornea is healed and the palpebral conjunctiva seems quiet, that is in about two weeks. If no reaction or infection is manifest it is best to leave the flap for three weeks or longer. The flap may be replaced whenever it becomes macerated or shredded.

Causes of Blindness in Pennsylvania.—Cowan and English state that since 1934, when an act granting pensions to blind persons in Pennsylvania was enacted, the causes for the blindness of 15,676 persons or 31,352 eyes have been tabulated. Persons 21 or older with a visual acuity of 20/200 (6/60) or less were considered industrially blind. This is the definition of blindness adopted by the Committee on Statistics of the Blind. The outstanding causes in the order of frequency were senile cataract, uveitis, glaucoma, trauma, congenital anomalies and neonatal ophthalmia. Since May 1939, when therapeutic procedures have been recommended the vision of 11.1 per cent of the persons with whom contact was established has been restored or improved. This has resulted in a substantial saving to the commonwealth in the payment of pensions.

Archives of Surgery, Chicago

43:735-932 (Nov.) 1941

*Treatment of Hypoproteinemia by Oral Administration of Protein Hydrolysate. C. A. Beling and R. E. Lee, Newark, N. J.—p. 735.
Regional Lymphatic Metastases of Carcinoma of Stomach. F. A. Coller, E. B. Kay and R. S. McIntyre, Ann Arbor, Mich.—p. 748.
Acute Cholecystitis. R. H. Wallace and A. W. Allen, Boston.—p. 762.
Alimentary Azotemia and Bleeding Peptic Ulcer Syndrome. C. F. Chunn, H. N. Harkins and R. T. Boals, Detroit.—p. 773.
Hydatid Disease (Hydatidosis): Hydatid Cyst of Lung. J. Arce, Buenos Aires, Argentina.—p. 789.
*Carcinoma of Upper Extremity. D. A. Campbell, Ann Arbor, Mich.—p. 803.
Intestinal Obstruction. J. K. Donaldson, E. B. Sive and N. Lewis, Little Rock, Ark.—p. 811.
Hodgkin's Disease: Review of Fifty-Four Cases. R. E. Burger and E. P. Lehman, Charlottesville, Va.—p. 839.
*Preoperative Management of Gastrojejunocolic Fistula. H. K. Gray and W. S. Sharpe, Rochester, Minn.—p. 850.
Congenital Duodenal Obstruction. C. S. White and J. L. Collins, Washington, D. C.—p. 858.

Protein Hydrolysate for Hypoproteinemia.—Beling and Lee point out that the feeding of a hydrolysate of proteins from beef, milk and wheat to 30 patients with hypoproteinemia satisfactorily replaced proteins in the plasma and corrected the various anomalies which accompanied the hypoproteinemia. Replacement was rapid but was not fast enough for the treatment of shock and immediate hypoproteinemia. The hydrolysate is valuable as an adjunct to intravenously administered plasma. Its preoperative and postoperative use is important in correcting hypoproteinemia before and in preventing its occurrence after gastrointestinal surgical procedures.

Carcinoma of Upper Extremity.—Campbell believes that carcinomas of the upper extremity, although not frequent, are too often underrated, overlooked or undertreated. A good prognosis is to be expected only if early treatment is vigorous. Among the 36 cases patients with the disease observed at the hospital of the University of Michigan 32 were men and 4 were women. At the initial examination, 44.4 per cent of the patients had palpable epitrochlear or axillary nodes or both, and 50 per cent suffered a recurrence or ultimately died of the carcinoma. Only 4 patients have lived five years or more without a recurrence. However, many of the patients died of intercurrent disease, without evidence of recurrence, before the five year limit was reached. In 18 patients proved unrelated cutaneous

neoplasms were present; fourteen were on the face and four on other extremities. Thirty-four of the carcinomas were of the squamous cell type, one was mediocellular and one was an adenocarcinoma of sweat gland origin. Operation and roentgen or radium irradiation remain the most popular procedures in the treatment of the local lesions and the involved lymph nodes. Although 15 of the 36 patients died, 7 died from causes attributed to the carcinoma and 8 from intercurrent disease. The average age of those dying from cancer was 52.7 years, and of those dying from intercurrent disease it was 75 years.

Gastrojejunocolic Fistula.—From a study of the 49 patients with gastrojejunocolic fistula operated on at the Mayo Clinic from 1930 to 1939 Gray and Sharpe conclude that the prohibitive mortality rate following one stage reparative procedures can be lowered materially by adequate preoperative management. Eighteen of the 49 patients died; of 13 receiving no preoperative preparation 8 died, and of 36 given fairly satisfactory preparation 10 died. However, only 1 of 7 having careful and adequate preoperative attention died.

Arkansas Medical Society Journal, Fort Smith

38:115-138 (Nov.) 1941

Regional Enteritis: Report of Case—Summary. J. B. Jameson, Camden.—p. 115.
Present Status of Sulfonamide Therapy. J. N. Compton, Little Rock.—p. 117.

Bulletin of Johns Hopkins Hospital, Baltimore

69:297-396 (Oct.) 1941

*Studies on Sulfadiazine: I. Chemotherapy of Experimental Hemolytic Streptococcic, Pneumococcic and Staphylococcic Infections in Mice. P. H. Long, Eleanor A. Bliss and E. Ott, Baltimore.—p. 297.
*Id.: II. Clinical Use of Sulfadiazine in Therapy of Bacterial Infections, Other Than Pneumonia. G. I. Trevett, R. A. Nelson and P. H. Long, Baltimore.—p. 303.
*Id.: III. Use of Sulfadiazine in Treatment of Pneumococcic Pneumonia. F. T. Billings Jr. and W. B. Wood Jr., Baltimore.—p. 314.
Experimental Shock: I. Effects of Acute Hemorrhage in Healthy Dogs. P. B. Price, C. R. Hanlon, W. P. Longmire and W. Metcalf, Baltimore.—p. 327.
Results of Artificial Pneumothorax Therapy in Pulmonary Tuberculosis. H. G. Whitehead, Baltimore.—p. 363.

Studies on Sulfadiazine.—Long and his colleagues after finding sulfadiazine effective in controlling experimental pneumococcic, staphylococcic and hemolytic streptococcic infections used it clinically for 230 patients with bacterial infections, including 105 with pneumonia. As relatively high concentrations of sulfadiazine can be maintained in the blood without frequent toxic reactions, the therapeutic result is better with this drug than it is with other sulfanilamide derivatives. For the mild or moderately severe hemolytic streptococcic infections (tonsillitis, erysipelas, otitis media, mild scarlet fever and the like) the authors prefer oral therapy. They base the inital dose on 0.05 Gm. per kilogram of body weight. Two of 3 patients ill with meningococcic meningitis responded favorably to the drug, while the other died within one hour after therapy was started. Of 6 patients with subacute bacterial endocarditis, 1 has made a dramatic response to therapy and the other 5 were not materially improved by chemotherapy. Five of the 12 patients with various types of staphylococcic infections (osteomyelitis) who were given sufficient doses of the drug to maintain a level in the blood of 5 to 7 mg. made a gratifying response to therapy, and all continued to take the drug for at least four months. From July 1940 to June 1941 105 adults with pneumonia have been treated with sulfadiazine alone or with sulfadiazine and type specific antipneumococcus serum. Of the 75 patients who received only sulfadiazine 56 had pneumonia due to pneumococci of types I to VIII, 7 had bacteremia, 8 had complications associated with the pneumonia and 14 had a major concurrent disease. Only 1 patient died, nine hours after entering the hospital. The response to sulfadiazine therapy was usually prompt, but it did depend, at least in part, on the concentration of sulfadiazine in the blood during the first twelve to twenty-four hours of treatment. Of the 30 patients with pneumococcic pneumonia treated with sulfadiazine and antipneumococcus serum 16 had positive blood cultures and 18 had major concurrent diseases. Seven patients died, of whom 6 had major concurrent diseases and 4 were in shock when admitted to the hospital. Only 17 of the 230 patients treated experienced toxic reactions.

Canadian Medical Association Journal, Montreal

45:295-384 (Oct.) 1941

*Treatment of Angina Pectoris of Atheromatous Origin by Ligation of Great Cardiac Vein. M. Fauteux and J. H. Palmer, Montreal.—p. 295.
Surgical Management of Gastric and Duodenal Ulcers. P. H. T. Thorlakson and A. W. S. Hay, Winnipeg, Man.—p. 298.
Prevention, Control and Treatment of Human Cancer as Deficiency Disease: Preliminary Report. J. R. Davidson, Winnipeg, Man.—p. 308.
Radiologic Study of Mastoids in Children. L. A. Gagnier Jr., Montreal.—p. 312.
Granulomatous Lymphadenitis Caused by Filariae. Miriam A. Brick and W. L. Donohue, Toronto.—p. 315.
*New Immunization Program in Royal Canadian Air Force. A. H. Sellers, Toronto.—p. 318.
Prognosis in Bilateral Renal Tuberculosis. W. F. Braasch and E. B. Sutton, Rochester, Minn.—p. 320.
Clinical Studies in Immunity to Pertussis with Use of Pertussis Skin Testing Toxin and Antiendotoxin. L. P. Strean, Montreal; D. Lapointe and E. Dechene, Quebec.—p. 326.
*Anuria: Report of Three Types of Cases. J. C. McClelland, Toronto.—p. 332.
Nail Polish Dermatitis. J. F. Burgess, Montreal.—p. 336.
Pain of Cancer from Neurosurgeon's Viewpoint. F. Turnbull, Vancouver, B. C.—p. 339.
Interstitial Cystitis. E. Smith and F. D. Conroy, Montreal.—p. 342.
Serious Injury to Rectum from Improperly Administered Enemas. H. C. Ballon and A. Goldbloom, Montreal.—p. 345.

Ligation of Great Cardiac Vein for Angina Pectoris.—Their experimental observations on dogs suggested to Fauteux and Palmer that venous ligation would be of considerable value in the treatment of advanced coronary disease in man. Consequently, on April 19, 1939, they operated on a patient with severe angina of effort. More than two years have elapsed since the operation, and the patient has been entirely free from pain. This relief the authors believe is due to an improvement in the coronary circulation rather than to any interruption of nervous pathways or danger signals. It is their opinion that at least for the present only patients with severe angina pectoris who have not responded to medical treatment should be operated on. In other words, until further experience is gained venous ligation should be reserved for angina pectoris of atheromatous origin rather than for coronary disease as such.

Immunization of Canadian Air Force.—Sellers states that outbreaks of diphtheria and scarlet fever among the air force personnel during the winter and spring of 1940-1941 caused procedures promising effective future control to be introduced. The program calls for Schick and Dick testing and subsequent immunization of all air force personnel throughout Canada and Newfoundland during the training period, before proceeding overseas where these diseases are more prevalent. By this procedure it can be expected that diphtheria will be almost completely eliminated from the air force personnel. For scarlet fever the ground is not so certain, but immunization is the best available weapon. All personnel either in or entering the service are Schick and Dick tested. The result of the Schick test is read in twenty-four or forty-eight hours, and if negative it is read again in five or seven days. All personnel with positive Schick reactions (on the first or the second reading) are given subcutaneously two 1 cc. doses, four weeks apart, of alum precipitated diphtheria toxoid. Schick-sensitive persons are not given toxoid. The Dick reaction is read in twenty-two or twenty-four hours, and all those showing a positive one are given five 1 cc. injections of scarlet fever toxin subcutaneously at weekly intervals in graded doses. Special clinics with trained personnel have been set up at large stations of initial entry. Permanent records of all tests and inoculations are made, and when immunization is complete the records are sent to air force headquarters to be used for statistical purposes.

Anuria.—McClelland discusses three types of anuria: anuria from sulfapyridine, from calculi on both sides and from crush injury in mines. Treatment must be directed at the cause. An obstructing calculus must be removed. If both ureters are blocked it is sufficient to remove the stone or stones from one side and to treat the other side expectantly. The one well functioning kidney is sufficient to sustain life and to bring the nitrogen content of the blood down to normal, and the obstruction of the other side can be treated when the patient's condition is improved. Hence it is the author's belief that unilateral anuria must occur more frequently than it is realized. The

shutting off of one kidney is evidently not important as long as the function of the other kidney is good. Ureteral obstruction due to sulfapyridine crystals can be overcome by the passage of ureteral catheters. Surgical intervention is indicated only if ureteral catheterization fails. There is no specific treatment for crush injuries. The intravenous administration of saline and dextrose solutions or dextrose in distilled water is useful. The dextrose should be made up in distilled water if the patient's nonprotein nitrogen level is more than 100 mg. Aminophyllin and caffeine with sodium benzoate should be used.

Endocrinology, Springfield, Ill.

29:483-654 (Oct.) 1941. **Partial Index**

Reaction of Human Chorionic and Equine Gonadotropins to Formaldehyde. F. Bischoff, Santa Barbara, Calif.—p. 520.
Selective Neutralization of Follicle Stimulating Action of Gonadotropic Preparations by Antigonadotropic Serums. H. S. Kupperman, R. K. Meyer and W. H. McShan, Madison, Wis.—p. 525.
Specificity of Pregnancy Urine Antiprolan with Respect to Human Gonadotropic Hormones from Various Sources. B. Zondek, F. Sulman and J. Sklow, Jerusalem, Palestine.—p. 531.
Desoxycorticosterone Acetate Requirement of Adrenalectomized Dog. R. A. Cleghorn, J. L. A. Fowler, J. S. Wenzel and A. P. W. Clarke, Toronto, Canada.—p. 535.
Attenuation of Insulin by Adsorption. J. M. Johlin.—p. 574.
Effect of Glycolysis Inhibitors and of Certain Substrates on Metabolism and Motility of Human Spermatozoa. J. MacLeod, New York.—p. 583.
Comparative Action of Stilbestrol and Other Estrogens on Endometrium of Castrated Guinea Pig. A. Lipschütz and L. Vargas Jr., Santiago, Chile.—p. 622.
Inhibition of Copper Induced Ovulation in Rabbit by Progesterone. M. H. Friedman, Beltsville, Md.—p. 628.
Action of Progesterone on Genital Organs of Unprimed Rhesus Monkey. C. G. Hartman and H. Speert, Baltimore.—p. 639.

Florida Medical Association Journal, Jacksonville

28:149-196 (Oct.) 1941

Labor in Abnormal Presentations. R. G. Nelson, Tampa.—p. 159.
Role of the Delivery Home in Treating the Low Income Group. J. M. Hoffman, Pensacola.—p. 162.
Toxemia of Pregnancy. S. R. Norris, Jacksonville.—p. 164.
Management of Primary Glaucoma. H. J. Blackmon, Tampa.—p. 169.
Practicing Physician's Place in Public Health. W. H. Pickett, Jacksonville.—p. 173.
Labor and the Industrial Surgeon. L. F. Carlton, Tampa.—p. 175.
Coordinating the School and Health Program. A. L. Stebbins, Pensacola.—p. 176.

Journal of Bone and Joint Surgery, Boston

23:753-1024 (Oct.) 1941. **Partial Index**

Aseptic Necrosis of Femoral Head Following Traumatic Dislocation of Hip: Report of Nine Cases. S. W. Banks, Chicago.—p. 753.
Significance of Phlebothrombosis and Thrombophlebitis in Orthopedic Surgery. A. Ochsner and M. DeBakey, New Orleans.—p. 788.
Simple Method of Ambulatory Treatment of Fractures of Clavicle. M. G. Kini, Vizagapatam, South India.—p. 795.
Bone Tuberculosis in Northern Newfoundland. C. S. Curtis and E. G. Loomis, St. Anthony, Newfoundland.—p. 811.
Retrolunar Dislocation of Capitate with Fracture or Subluxation of Navicular Bone. E. F. Cave, Boston.—p. 830.
Conservative and Operative Treatment of Fractures of Carpal Scaphoid (Navicular). R. Soto-Hall and K. O. Haldeman, San Francisco.—p. 841.
Evaluation of Physiotherapy in Early Treatment of Anterior Poliomyelitis. H. R. McCarroll and C. H. Crego Jr., St. Louis.—p. 851.
*Gradation of Ewing's Tumor (Endothelial Myeloma). W. C. Campbell and J. F. Hamilton, Memphis, Tenn.—p. 869.
Scoliosis Complicated by Spinal Cord Involvement. C. W. Ruhlin, Bangor, Maine, and S. Albert, Iowa City.—p. 877.
*Fractures of Tibia in Adults. S. S. Hudack, New York.—p. 896.
Review of 201 Cases of Suppurative Arthritis. J. A. Heberling, Pittsburgh.—p. 917.
Carpal Boss: Commonly Overlooked Deformity of Carpus. R. M. Carter, Green Bay, Wis.—p. 935.
Roentgenographic Recognition of Synovioma. A. P. Aitken, Boston.—p. 950.
*Conservative Treatment of Serratus Palsy. J. Wolf, Davenport, Iowa.—p. 959.

Gradation of Ewing's Tumor.—In studying the cellular activity of thirty Ewing tumors Campbell and Hamilton tried to divide them into grades, according to the number of mitotic figures observed in a high power field: grade 1, one to five figures; grade 2, six to ten figures, and grade 3, eleven to fifteen figures. It appears to the authors that a patient with a tumor having five or less mitotic figures has approximately a 23 per cent chance to survive ten years and a 31 per cent chance to live five years, whereas if the count is eleven or more he will probably not live for much longer than one year. None of the authors' patients with grade 2 tumors lived ten years, but 3, or 33 per cent, lived more than five years. Roentgenograms of the thirty tumors indicate that the early stage of the tumor, characterized by osseous condensation, is concomitant with increased cellular activity, whereas late osseous changes are usually accompanied by diminished cellular activity. Studies of large numbers of cases might throw more light on the subject and lead to the discovery of a method of establishing a more accurate prognosis.

Fractures of Tibia in Adults.—Hudack compared the operative and nonoperative treatment of eighty-two tibial fractures in adults treated from 1929 to 1938. He found that operative treatment gave assurance of a surer course and better results than did nonoperative treatment.

Conservative Treatment of Serratus Palsy.—Wolf describes a brace for patients with permanent paralysis of the serratus muscle that allows complete use of the arm, presses the winged scapula in its normal position against the wall of the chest and prevents scapular rotation.

Journal of Clin. Endocrinology, Springfield, Ill.

1:711-788 (Sept.) 1941

Acute Atrophy of Bone (Osteoporosis) Simulating Hyperparathyroidism. F. Albright, C. H. Burnett, O. Cope and W. Parson, Boston.—p. 711.
Linear Growth and Epiphysial Closure: Effect of Treatment with Chorionic Gonadotropic Substance—Report of Twenty-Three Cases. L. A. Lurie and J. Hertzman, Cincinnati.—p. 717.
Von Recklinghausen's Disease with Diabetes Mellitus. S. R. Halpern and Gladys J. Fashena, Dallas, Texas.—p. 726.
Effect of Various Gonadotropins on Spermatogenesis and Urinary Androgens in the Human. E. P. McCullagh and E. J. Ryan, Cleveland.—p. 728.
Endocrine Therapy of Functional Menometrorrhagia and Ovarian Sterility: III. Cyclic Administration of Equine Gonadotropin. E. C. Hamblen, W. K. Cuyler, J. A. Wilson and R. L. Pullen, Durham, N. C.—p. 742.
Id.: IV. One-Two Cyclic Therapy with Equine and Chorionic Gonadotropins. E. C. Hamblen, W. K. Cuyler, J. A. Wilson and R. L. Pullen, Durham, N. C.—p. 749.
Use of Estrogenic Vaginal Suppositories in Vaginitis in Women. L. Neugarten and E. Steinitz, New York.—p. 754.
Suitable Dosage of Stilbestrol for Suppression of Lactation. J. Clahr, Bronx, N. Y.—p. 759.
Urinary Excretion of 17-Ketosteroids in Ovarian Failure: Parts I to IV. E. C. Hamblen, W. K. Cuyler and Margaret Baptist, Durham, N. C.—p. 763.
Increased Excretion of Gonadotropic Hormone in Pregnant Woman with Mammary Carcinoma. B. Zondek, Jerusalem, Palestine.—p. 782.
Correlation of Fetal Adrenal Glands with Edema and Toxemia of Late Pregnancy. T. J. Parks, New York.—p. 784.

1:789-858 (Oct.) 1941

Studies on Convulsive Mechanism in Idiopathic Hypoparathyroidism. I. McQuarrie, A. E. Hansen and M. R. Ziegler, Minneapolis.—p. 789.
Sterol Balance in Hypothyroidism. W. Fleischmann and L. Wilkins, with technical assistance of E. Smetana, Baltimore.—p. 799.
Clinical Applications of Studies in Experimentally Induced Exophthalmos of Anterior Pituitary Origin. H. B. Friedgood, Boston.—p. 804.
Gonadotropic Hormone: Urine Assays During Menstrual Cycle in Normal Women. Emily J. Heller, Madison, Wis.—p. 813.
*Relation of Dose and Type of Estrogen to Nausea and Vomiting. R. R. Greene and E. M. Dorr, Chicago.—p. 821.
Effect of Desoxycorticosterone Acetate on Glucose Tolerance in Normal Individuals and in Patients with Addison's Disease. T. H. McGavack, G. P. Charlton and S. Klotz, New York.—p. 824.
Intensive Carbohydrate Therapy in Diabetic Patients with Manifest or Suspected Liver Disease. C. D. Strouse, E. E. Rosenbaum, R. C. Levy and S. Soskin, Chicago.—p. 831.
Thyroid Globulin in Treatment of Menstrual Irregularities. Ruth C. Foster and M. A. Foster, Madison, Wis.—p. 836.
*Treatment of Recurrent and Threatened Abortion: Report of 226 Cases. J. Kotz, Elizabeth Parker and M. S. Kaufman, Washington, D. C.—p. 838.

Relation of Estrogen to Nausea and Vomiting.—Greene and Dorr present evidence that there is a definite relationship between the amount of diethylstilbestrol administered and the incidence of nausea and vomiting. They gave 283 women in the menopause diethylstilbestrol and related stilbene derivatives orally or parenterally. Reactions were more frequent with larger doses. The incidence of reactions was high with diethylstilbestrol, which is relatively rapidly absorbed from the site of injection. Reactions were less frequent with stilbestrol dipropionate, which is relatively slowly absorbed. Giving diethylstilbestrol orally should control menopausal symptoms and should

not cause reactions if excessive amounts are avoided. If treatment is started with a daily 0.1 mg. dose, increased after one or two weeks to 0.2 mg. and then after each succeeding one or two weeks raised to 0.5, 1, 1.5 and 2 mg. until symptomatic improvement is obtained and maintained, reactions will be reduced to a minimum. Only 22.5 per cent of the authors' patients needed doses larger than 0.5 mg. None of their patients had undesirable side reactions.

Progesterone for Threatened Abortion.—Kotz and his associates used progesterone for the treatment of 181 of 226 women whose pregnancy appeared to be threatened. Forty-two women received progesterone prophylactically (36 gave a history of one or more previous unsuccessful pregnancies, and 6 had been treated for primary sterility). The bleeding of the 45 patients who received no progesterone was slight and its duration so short that treatment did not seem warranted, or the patients were seen so late that treatment was considered useless. Of the 6 patients with primary sterility, 1 bled during pregnancy but went to near term and gave birth to a viable premature infant, and the other 5 had normal full term infants with no evidence of abnormality. The 36 patients had had a total of seventy-two pregnancies terminating in the birth of 8 full term infants. Under treatment, 28 carried through to term without bleeding, 3 had some bleeding and 5 aborted. The 3 patients with some bleeding went into labor and were delivered of viable infants two or more weeks prior to the expected date of confinement. Of 184 women who bled during the first eight months of gestation 139 were given progesterone; 102 of them were delivered of viable infants, while 82 aborted. The infants of 16 of the 102 patients who gave birth to viable babies were two or more weeks premature. Among the 184 women 91, or 49.4 per cent, had their first or only episode of bleeding in the second month of pregnancy, and of these 42, or 46.1 per cent, aborted. In the third month there were 56, or 30.4 per cent, and of these 31, or 55.3 per cent, aborted. The authors suggest that probably many abortions that physicians do not know about occur in the first month of pregnancy, as the women do not come for medical care. They believe their data demonstrate that if progesterone is to be given prophylactically its administration should be started early, certainly in the first month, and continued at least through the third month; the dose should be increased and other precautionary measures taken at the expected time of the second, third and fourth missed menstrual periods. The danger of abortion does not disappear after the third month even though the placenta takes over the production of progesterone. The hormone imbalance persists in a few women, and the continued use of progesterone benefits these women. Patients with sterility, women who habitually abort and those who have bled during the pregnancy should have prophylactic treatment continued at least until the end of the fifth month and preferably to term. There are at least three factors, probably interactive, which may cause abortions: defective germ plasm, endocrine deficiencies and nutritional deficiencies. No amount of therapy will affect the first cause, but the second and third causes may be amenable to treatment. The problem is to recognize them and to treat patients with these deficiencies adequately.

Journal of Immunology, Baltimore

42:1-108 (Sept.) 1941

Immunologic Relationship Between Spotted Fever and Exanthematic Typhus. M. Ruiz Castaneda and R. Silva, Mexico City, Mexico.—p. 1.

Cross Protection Between Heterologous Agglutinogenic Types of Beta Hemolytic Streptococci. Alice C. Evans, Washington, D. C.—p. 15.

Blood Constituents During Anaphylactic Shock in Monkey. L. W. Kinsell, L. M. Kopeloff, R. L. Zwemer and N. Kopeloff, New York.—p. 35.

Use of Chick Embryo Tissues and Fluid as Antigens in Complement Fixation Reaction in Influenza. Clara Nigg, J. H. Crowley and Doris E. Wilson, Minneapolis.—p. 51.

Occurrence of Forssman Heterogenetic Antigen in Nematode Trichinella Spiralis. Evelyn Abrams Mauss, Baltimore.—p. 71.

Relationship Between Constant-Antiserum and Constant-Antigen Optimal Ratios Obtained with Rat and Guinea Pig Precipitin. Charlotte A. Colwell and G. P. Youmans, Chicago.—p. 79.

Serologic and Biochemical Study of Hemolytic Streptococci. Helen Plummer, Toronto, Canada.—p. 91.

Journal of Investigative Dermatology, Baltimore

4:259-330 (Aug.) 1941

Statistical Analysis of Spore Size in Genus Microsporum. N. F. Conant, Durham, N. C.—p. 265.

Technic for Measuring Oxidation-Reduction Potential of Skin and Other Surfaces. Rita M. Kelley and J. W. Williams, Cambridge, Mass.—p. 279.

Hereditary Dystrophy of Hair and Nails. T. Benedek, Chicago.—p. 285.

Studies in Adhesive Tape Irritation. J. M. Sheldon, Hilda M. Hensel and F. Blumenthal, Ann Arbor, Mich.—p. 295.

Relationship Between Acid-Base Equilibrium and Endogenous Bacterial Flora of Skin. Frances Creekmur Whitcomb and L. Arnold, Chicago.—p. 317.

Effect of Monobenzyl Hydroquinone on Oxidase Systems in Vivo and in Vitro. S. M. Peck and H. Sobotka, New York.—p. 325.

4:331-430 (Oct.) 1941

Mitoses Occurring in Acanthosis Produced by Hormones. E. Uehlinger, W. Jadassohn, Zurich, Switzerland, and H. E. Fierz, St. Gaul, Switzerland.—p. 331.

Poison Ivy Plant and Its Oleoresin. B. Shelmire, Dallas, Texas.—p. 337.

Artificial Blister in Study of Eosinophils, with Particular Reference to Dermatitis Herpetiformis. M. H. Goodman, Baltimore.—p. 349.

Epithelioma Attributable to Arsenic. H. Montgomery, Rochester, Minn., and M. Waisman, Chicago.—p. 365.

Vitamin Deficiency Syndrome in Albino Rat Precipitated by Chronic Zinc Chloride Poisoning. P. Gross, Z. Harvalik and Edith Runne, New York.—p. 385.

Investigations Concerning Actual Methods Employed in Management of Common Dermatoses: Practical Management of Psoriasis. S. Ayres Jr., Los Angeles; S. W. Becker, Chicago; L. Chargin, New York; T. Cornbleet, Chicago; E. C. Fox, Dallas, Texas; J. F. Madden, St. Paul, and P. A. O'Leary, Rochester, Minn.—p. 399.

Journal of Pharmacology & Exper. Therap., Baltimore

73:119-228 (Oct.) 1941. **Partial Index**

Potentiation of Acetylcholine by Alcohol and Ether. G. H. Ettinger, A. B. Brown and A. H. Megill, Kingston, Ont., Canada.—p. 119.

Studies Concerning Anesthetic Action of Steroid Hormones. H. Selye, Montreal, Canada.—p. 127.

Effect of Sodium Amytal on Emptying Time of Normal Human Stomach. E. J. Van Liere and D. W. Northrup, Morgantown, W. Va.—p. 142.

Effect of Atabrine on Experimental Cysticercosis of Mice. J. T. Culbertson and Sylvia H. Greenfield, New York.—p. 159.

Depression of Experimental Polycythemias by Various Substances in Dogs, Rabbits and Man. J. E. Davis, Burlington, Vt.—p. 162.

Studies on Acute Toxicity of Sulfacetimide (Para-Aminobenzene Sulfonyl Acetyl Imide). R. Donovick and E. Henderson.—p. 170.

Therapeutic Effect of Sulfacetimide in Experimental Infections Due to Escherichia Coli. R. Donovick and E. Henderson.—p. 173.

Relative Activity of Digitalis Preparations in Frog, Cat and Man, and Its Bearing on Problem of Bioassay and So-Called Deterioration. H. Gold, M. Cattell, N. T. Kwit and M. Kramer.—p. 212.

Kansas Medical Society Journal, Topeka

42:413-456 (Oct.) 1941

Office Treatment of Anorectal Diseases and Its Limitations. L. J. Hirschman, Detroit.—p. 413.

Diagnosis and Treatment of Early Congestive Heart Failure. C. W. Erickson, Pittsburg.—p. 418.

Study of Leukorrhea in General Practice. C. W. Haines, Haven.—p. 422.

Sodium Hypochlorite Dermatitis. M. Bernreiter, Kansas City.—p. 424.

Intravenous Anesthesia. H. R. Schmidt, Newton.—p. 425.

Relapsing Fever. H. O. Closson, Ashland.—p. 427.

Systemic Action of Drugs Placed on Intact Skin. P. W. Miles, Newton.—p. 430.

Cholecystography in Presence of Jaundice. M. H. Delp, Kansas City.—p. 434.

Laryngoscope, St. Louis

51:903-982 (Oct.) 1941

Rhinogenic Retrobulbar Neuritis. H. Brunner, Chicago.—p. 903.

What Was Wrong with Otolaryngology in the Last War. H. P. Mosher, Marblehead, Mass.—p. 930.

Hearing Standards for Acceptance, Disability Rating and Discharge in Military Services and in Industry. E. P. Fowler, New York.—p. 937.

*Management of [Military] Injuries to Middle and Internal Ear Including Fractures of Temporal Bone. W. E. Grove, Milwaukee.—p. 957.

Prevention and Treatment of Acoustic Trauma in War and Civil Life. D. Macfarlan, Philadelphia.—p. 964.

Malingering and Neuro-Otologic Considerations in Combat Services. E. R. Lewis, Los Angeles.—p. 970.

The Ear in Flying. J. R. Poppen, Washington, D. C.—p. 974.

Injuries to Middle and Internal Ear.—Grove states that the tympanic membrane may be ruptured by the direct penetration of a foreign body, by the extension of a fracture of the temporal bone and by the condensation or rarefaction of air in the external auditory canal. Traumatic ruptures not associated

with fractures of the basal part of the skull usually heal by first intention and should be treated conservatively and expectantly. If suppuration of the middle ear supervenes, time-honored methods are to be used. Suppuration of the middle ear almost always follows perforations of the drum caused by burns, and often the perforation is persistent. Suppuration rarely occurs, except when encouraged by bad management, in rupture of the drum caused by a sudden elevation of air pressure in the external canal. If fracture of the temporal bone is followed by a discharge of blood or cerebrospinal fluid from the ear, nothing should be done except to place sterile cotton in the meatus and to cover the ear with sterile dressings. After a few days, if the bleeding persists, the sterile dressings should be changed. The ear should never be cleansed in less than two or three weeks and then should be cleansed mechanically with sterile instruments. Even at this date the ear should not be irrigated, because the tympanic membrane may still be perforated. If the sigmoid sinus has been injured it should be exposed and then blocked. When a fracture of the basal part of the skull exists, its treatment is of first importance. Of the three stages (shock, increasing intracranial pressure and medullary failure) to be recognized and treated in patients with severe injuries of the head the treatment of the shock should take precedence. The indications for operation are compound fractures of the skull or fractures which involve noticeable depression, extradural hemorrhage, increased intracranial pressure not improving under medical treatment and definite local paralysis or convulsions. Medical treatment consists of (1) absolute rest in bed for three to six weeks, (2) elevation of the head and trunk, (3) administration of drugs (caffeine with sodium benzoate to lower intracranial pressure and bromides and barbiturates to control restlessness), (4) dehydration (with the giving of magnesium sulfate, the intravenous administration of hypertonic solutions of sucrose or dextrose and the limitation of the fluid intake) and (5) repeated lumbar punctures to lower intracranial pressure and to remove blood from the subarachnoid spaces. Morphine tends to increase intracranial pressure and should never de administered.

New England Journal of Medicine, Boston

225:561-600 (Oct. 9) 1941

The Open Safety Pin: Consideration of Its Peroral Removal from Upper Air and Food Passages. L. G. Richards, Boston.—p. 561.
Enlargement of Heart. P. D. White, Boston.—p. 571.
Nutrition in War. R. S. Harris, Cambridge, Mass.—p. 575.
Arteritis: Diseases Associated with Inflammatory Lesions of Peripheral Arteries. S. Weiss, Boston.—p. 579.

225:601-636 (Oct. 16) 1941

Some Uses and Abuses of Chemotherapy in Pneumonia. M. Finland, O. L. Peterson and E. Strauss, Boston.—p. 601.
Carcinoma of Endometrium: Review with Results of Treatment Through 1935. G. Van S. Smith, Brookline, Mass.—p. 608.
Glaucoma and the General Practitioner. P. A. Chandler, Boston.—p. 615.
Surgical Care and Operative Technic. J. D. Stewart, Buffalo.—p. 620.

225:637-674 (Oct. 23) 1941

Role of Roentgenologic Examination in Diagnosis of Intestinal Obstruction. E. P. Pendergrass, Philadelphia.—p. 637.
Indications for Use of Miller-Abbott Tube. W. O. Abbott, Philadelphia.—p. 641.
Diagnosis and Management of Acute Obstruction of Small Intestine. L. S. McKittrick, Boston.—p. 647.
*Treatment of Tetanus. E. M. Chapman and R. H. Miller, Boston.—p. 652.
General Anesthesia. Priscilla Sellman and U. H. Eversole, Boston.—p. 657.

Treatment of Tetanus.—Chapman and Miller report the successful outcome of therapy in a case of severe tetanus. The original injury, in a boy of 10, occurred on an ocean beach; tetanus ensued six days later. The authors believe that the six point program of treatment employed was responsible for the recovery of the child. The six features were profound sedation, surgical removal of the focus of infection, moderate intravenous doses of tetanus antitoxin, frequent lumbar punctures, maintenance of an adequate respiratory exchange and the most intelligent and constant nursing care.

Ohio State Medical Journal, Columbus

37:1029-1132 (Nov.) 1941

Cardiac Disease and Foci of Infection. N. P. Frolkis, Akron.—p. 1045.
Surgery for Patient with Disease of Thyroid and Impairment of Heart. J. M. Miller, Marion.—p. 1048.
Pernoston, Intravenous Barbiturate. B. R. Bonnot, Canton.—p. 1050.
Laryngeal Carcinoma. J. W. McCall, Cleveland, and A. J. Lamb, East Cleveland.—p. 1053.
Spontaneous Interstitial Emphysema of Lungs: Report of Two Cases and Summary of Literature. I. Miller, Urbana.—p. 1056.
*"Trigeminal Neuralgia" as Complication of Prophylactic Use of Tetanus Antitoxin: Case Report. M. Rosenbaum, Cincinnati.—p. 1060.
Discussion of Orthoptic Training. C. J. Streicher, Canton.—p. 1062.
*Mastoiditis Without Classic Symptoms. F. W. Dixon, Cleveland.—p. 1065.
Adenocarcinoma of Sigmoid Colon, Rectum and Anus in Children: Report of Two Cases in a Thirteen Year Old Girl and an Eight Year Old Boy with Summary of Recorded Cases up to Fifteen Years of Age. M. Oosting, Dayton.—p. 1067.
Present Views on Shock. H. S. Applebaum, Cleveland.—p. 1069.
Endocrinology in Gynecologic Practice. A. G. Sar-Louis, Cleveland.—p. 1073.
Cavernous Sinus Thrombosis: Recovery Following Treatment with Sulfathiazole. J. P. Eichhorn, Fort Benjamin Harrison, Ind.—p. 1076.
Ruptured Diverticulum of Ileum: Case Record Presenting Clinical Problems. S. Koletsky, Cleveland.—p. 1078.
Management of Acne Vulgaris. J. E. Rauschkolb, Cleveland.—p. 1079.
Ambulance. F. A. Riebel, Columbus.—p. 1081.

"Trigeminal Neuralgia" Following Tetanus Antitoxin.—Rosenbaum reports the occurrence of "trigeminal neuralgia" following an injection of tetanus antitoxin. The patient, a foreman in a tool and die making plant, sustained a cut on his left forearm. The wound was immediately treated, and a hypodermic injection of tetanus antitoxin was given into the deltoid region of the left arm. (The patient "argued against the injection" because of a reaction to an intra-abdominal injection of tetanus antitoxin fifteen years previously.) The day after the injection the left upper arm became swollen and painful. This subsided in about two weeks. About two days after the injection headache and severe nuchal pain developed and lasted for three weeks. A few days after the headache and nuchal pain had subsided the patient had a sudden severe attack of "shooting" pain in the left side of his face. The attack subsided after one hour. Ten days later a similar attack ensued. This attack subsided abruptly after two hours, during which time the patient was given two injections of morphine sulfate. A third, similar, attack, lasting two hours and unrelieved by morphine, occurred six days later and a fourth attack within two days more. The patient inhaled trichlorethylene during the fourth attack, without relief. The history was irrelevant except for the reaction fifteen years before. A few days after this injection large urticarial wheals developed around the site of the injection, and for about six months the anterior surface of the abdominal wall remained so painful that the patient was unable to wear a belt or fasten the upper buttons of his trousers. Ten months after the last attack of "trigeminal neuralgia" the patient has been free of attacks and in perfect health. The close association between the "attacks" and the "meningitic" reaction (headache and nuchal pain) suggested irritation of the roots of the second and third division of the left fifth cranial nerve.

Mastoiditis Without Classic Symptoms.—Dixon states that he encountered 6 cases of atypical mastoiditis in a period of three months. Five of the patients recovered; 1 died. There was no history of an acute infection of the upper part of the respiratory tract. With the exception of 1 patient, whose discomfort began six months before operation, the patients had been ill between four and five weeks. In only 2 instances was there transient slight tenderness to deep pressure. Examination of the external auditory canal showed a narrowing of the canal anteroposteriorly in 3 instances and an elevation of the floor in 2, and in 1 the lumen of the canal was normal. The tympanic membrane was dull, red, thickened and slightly bulging on the patients' first visit. The tympanic membranes of 2 patients with more pronounced bulging were opened, but only blood was discharged for twenty-four hours. One symptom, deep bone ache, was common to all the patients. The pain was constant, and codeine and morphine were required to relieve it. This pain and the distortion of the canal and the drum were the only pathologic indications. The patient who did not recover was first seen ten days prior to his death. His discomfort, deep-seated pain in

and about the ear, had begun two weeks previously. The floor of the canal seemed elevated. The drum was thickened and red but not bulging. During the ten days he performed his usual duties as a butcher, the canal became less swollen, the tympanic membrane lost its redness and the mastoid pain disappeared. The hearing improved. When last seen by the author the patient stated that he did not feel it necessary to return for observation. That night he suddenly became irrational, vomited and showed signs of cerebellar irritation. He was brought to the hospital unconscious. The mastoid cavity was opened. Under a dense cortex, a large perisinal abscess had ruptured into the posterior fossa. Despite blood transfusions and chemotherapy, the patient died within forty-eight hours. This man was the first patient of the series and, the author believes, should have been operated on when first seen. The other 5 patients were operated on with only the deep-seated persistent pain and a dull, thickened drum to indicate operation. The agent of the infection was not established, although routine bacteriologic studies were made. Cultures on brain broth and blood agar of the exudate from the mastoid of 1 patient yielded Staphylococcus aureus and Staphylococcus albus. The presence of the latter and the fact that all the other direct smears were sterile suggest contamination. The spinal fluid from the patient who died contained the type III pneumococcus.

Public Health Reports, Washington, D. C.

56:2033-2064 (Oct. 17) 1941

Public Health Administrator's Responsibility in Field of Occupational Disease Legislation. J. J. Bloomfield and W. M. Gafafer.—p. 2033.
*Strain of Rocky Mountain Spotted Fever Virus of Low Virulence Isolated in Western United States. N. H. Topping.—p. 2041.
Electrostatic Method for Collecting Bacteria from Air. C. M. Berry.—p. 2044.
Disabling Morbidity Among Industrial Workers, Second Quarter of 1941, with Note on Occurrence of Pneumonia Among Iron and Steel Workers. W. M. Gafafer.—p. 2052.

56:2065-2104 (Oct. 24) 1941

Plans for Handling Special Health and Other Problems Incident to Army Maneuvers in Tennessee. W. C. Williams and G. F. McGinnes.—p. 2065.
Health Status of Adults in Productive Ages. D. E. Hailman.—p. 2071.
New Method for Viewing Sheet Kodachrome. A. A. Stone, R. D. Reed and L. Schwartz.—p. 2087.

Rocky Mountain Spotted Fever Virus of Low Virulence.—Topping reports the isolation in the West of a strain of Rocky Mountain spotted fever virus of low virulence. The patient was seen in a hospital in Denver on May 23, 1940. He had been in Wyoming and had arrived in Denver on May 20. On this day a tick was found embedded in an old appendectomy scar and removed by a local physician. On the evening of May 21 the patient had severe chills, headache, muscular pains and, he believed, fever. The next morning he was admitted to the hospital. On May 23 he had a temperature of 103.4 F. and a maculopapular rash. Blood was drawn, and after it had clotted it was macerated in sterile saline solution, and the equivalent of about 4 cc. of whole blood was injected intraperitoneally into 2 guinea pigs. After a prolonged incubation period fever developed in 1 of these guinea pigs, from which the L strain of Rocky Mountain spotted fever was isolated. The strain has been passed through twenty-five generations of guinea pigs. Of 191 animals used 56 were killed either for transfer or for pathologic examination. There were 6 deaths among the remaining 135 guinea pigs, a fatality rate of 4.4 per cent. The rate is considerably lower than that for the mildest strain so far isolated in the East, which has a fatality rate of 8 per cent. Cross immunity tests have been done, and the L strain has given complete cross immunity with the B. R. strain of spotted fever and with the W strain. Other than the lengthened incubation period, the lack of scrotal involvement and a negligible fatality rate the L strain is indistinguishable from the usual strains isolated in the East. The author suggests that the geographic classification be dropped and that in the future strains of Rocky Mountain spotted fever be classified with reference to their high or low virulence for guinea pigs.

Rhode Island Medical Journal, Providence

24:181-198 (Oct.) 1941

Meditationes Medicorum. W. Pickles, Providence.—p. 181.
Intercapillary Glomerular Sclerosis: Diabetes Nephrosis Syndrome. B. E. Clarke, Providence.—p. 190.

Rocky Mountain Medical Journal, Denver

38:753-832 (Oct.) 1941

Treatment of Peptic Ulcer Based on Physiologic Principles. A. Ochsner and M. DeBakey, New Orleans.—p. 768.
Hypoglycemic Shock Followed by Secondary Hyperglycemia: Report of Case with Postmortem Findings. O. J. LaBarge, New Orleans, and O. A. Ogilvie, Salt Lake City.—p. 783.
Hemolytic Streptococcus Infections—Their Importance in Acute and Chronic Disease. C. S. Keefer, Boston.—p. 789.

Southern Surgeon, Atlanta, Ga.

10:773-848 (Nov.) 1941

Surgery of Biliary Tract. F. M. Douglass, Toledo, Ohio.—p. 773.
Principles Governing Diagnosis and Treatment of Acute Craniocerebral Injuries. C. Pilcher, Nashville, Tenn.—p. 783.
Traumatic Fistula of Stenson's Duct. M. B. Welborn, Evansville, Ind.—p. 793.
Relief of Contractures of Knee Following Extensive Burns. W. G. Hamm and J. H. Kite, Atlanta, Ga.—p. 795.
Survey of 496 Cases of Vaginal Bleeding. A. E. Imler, Philadelphia.—p. 802.
More Effective Surgical Mask. E. J. Poth, Baltimore.—p. 810.
Carcinoma of Ovary. H. R. Shands and R. L. Clark Jr., Jackson, Miss.—p. 813.
Osteitis Fibrosa Cystica. I. M. Wise, Mobile, Ala.—p. 819.
Tuberculosis of Breast. W. P. Nicolson Jr., Atlanta, Ga., and C. E. Gillespie, Memphis, Tenn.—p. 825.

Wisconsin Medical Journal, Madison

40:881-1012 (Oct.) 1941

Century of Progress in Wisconsin Medicine. G. Gundersen, La Crosse.—p. 895.
*Use of Venesection in Treatment of Erythremia. A. A. Holbrook, Milwaukee.—p. 899.
Clinical Value of Certain Laboratory Blood Tests. J. A. Schindler, Monroe.—p. 911.
Silicosis. A. J. Lanza, New York.—p. 923.
Tetanus with Recovery. L. C. Pomainville, Wisconsin Rapids, and L. M. Morse, Milwaukee.—p. 926.
Testosterone in Treatment of Testicular Deficiency and Prostatic Enlargement. W. M. Kearns, Milwaukee.—p. 927.

Venesection for Erythremia.—Holbrook withdrew from 125 to 750 cc. of blood from 10 patients with erythremia. He found that the venesection promptly relieved headache, nervousness, palpitation and sensations of heat and reduced, at least temporarily, the erythrocyte count, hemoglobin content and viscosity. The duration of the remissions varied; the extremes were a few days and a year. Generally venesection afforded subjective benefit for about two months. The withdrawal of lesser quantities (350 to 450 cc.) of blood seemed more effective than the withdrawal of larger ones (700 to 750 cc.). Failure to effect any symptomatic change for good or bad through venesection occurred after five (in as many patients) of the thirty-seven venesections performed. Blood viscosity tests furnish a reliable means for following the progress of patients under treatment. The results should be checked against erythrocyte counts from time to time. No reticulocyte responses were encountered in fifteen tests made after the withdrawal of 350 to 750 cc. of blood.

Yale Journal of Biology and Medicine, New Haven

14:1-120 (Oct.) 1941. **Partial Index**

Hippocrates and the Island of Cos. R. H. Major, Kansas City, Mo.—p. 1.
Secretion of Sulfonamide Drugs in Gastric Juice. M. Cooke, Rochester, N. Y.; H. W. Davenport, and L. S. Goodman, New Haven, Conn.—p. 13.
Factors in Resistance to Tuberculosis. B. Gerstl and R. Tennant, New Haven, Conn.—p. 29.
Rupture of Graafian Follicle and Corpus Luteum Cyst Simulating Appendicitis: Report of Forty-Two Cases. P. D. Keller and P. D. Rosahn, New Haven, Conn.—p. 45.
Influence of Chronic Vitamin A Deficiency on Bacterial Flora of Rats. C. G. Burn, Brooklyn; A. U. Orten, and A. H. Smith, Detroit.—p. 89.
Application of Falling-Drop Method for Specific Gravity Measurement to Determination of Serum Albumin. P. H. Barbour Jr., Brooklyn.—p. 107.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

22:179-240 (Aug.) 1941

Experiments on Cancerization of Cells in Vitro by Means of Rous Sarcoma Agent. L. Halberstaedter, L. Doljanski and E. Tenenbaum.—p. 179.

Formation of Protein Complexes in Heated Solutions of Rabbit Serum Proteins. A. Kleczkowski.—p. 188.

Effect of Heat on Flocculating Antibodies of Rabbit Antiserums. A. Kleczkowski.—p. 192.

Some Properties of Complexes Formed When Antigens Are Heated in Presence of Serologically Unspecific Proteins. F. C. Bawden and A. Kleczkowski.—p. 208.

Simplified Method for Estimation of Sulfanilamide and Sulfapyridine in Biologic Fluids. L. D. Scott.—p. 220.

Effects of Sodium Hexametaphosphate (Calgon) on Complement Action of Serum. J. Gordon and W. R. Atkin.—p. 226.

Studies on Effect of Carcinogenic Hydrocarbons on Immunity Reactions. C. Hoch-Ligeti.—p. 233.

Journal of Pathology and Bacteriology, Edinburgh

53:161-326 (Sept.) 1941

Chronic Renal Disease, Secondary Parathyroid Hyperplasia, Decalcification of Bone and Metastatic Calcification. Freda K. Herbert, H. G. Miller and G. O. Richardson.—p. 161.

Effects of Sulfanilamide, Sulfathiazole and Sulfapyridine on Development of Granulation Tissue and Their Toxic Action on Striped Muscle. L. E. Glynn.—p. 183.

Growth of Coliform Bacilli in Distilled Water. J. W. Bigger and J. H. Nelson.—p. 189.

Malignant Hypertension Associated with Hydatid Disease of Kidney. J. Davson.—p. 207.

Effect of Prontosil Therapy on Antistreptolysin O Titer in Rabbits During Immunization. C. A. Green.—p. 213.

*Observations on Antistreptolysin O Titer in Relation to Mechanism of Acute Rheumatic Fever. C. A. Green.—p. 223.

Reversed Passive Skin Sensitization to Horse Serum in Human Beings. G. P. Wright and S. J. Hopkins.—p. 243.

Adhesiveness of Blood Platelets in Normal Subjects with Varying Concentrations of Anticoagulants. Helen Payling Wright.—p. 255.

*Giant Cell Chronic Arteritis. J. R. Gilmour.—p. 263.

Antistreptolysin O in Acute Rheumatism.—Green determined the antistreptolysin O titers of the serum from 1,346 adolescent boys: The mean titer in normal controls was 79; in 82.3 per cent it was less than 125 units. In scarlatina the mean titer was raised to 300, with maximal titers occurring in the third and fourth weeks of infection. In simple pharyngitis due to Streptococcus hemolyticus the mean was 263. The mean titer in the active phase of acute rheumatism was 444 and during the inactive phase it was 210. Of one hundred and ten attacks of acute rheumatism, 79.9 per cent were accompanied by a significant increase in the titer, which usually reached maximal proportions at or just after the height of clinical activity, in 10.1 per cent there was no change in the titer and in 3.6 per cent the titer was reduced during the active phase. Either the few patients with acute rheumatism in whom there was no increase in the titer were similar to nonrheumatic patients who failed to react to infection by antibody production or else the infection had no part in inducing the rheumatic state.

Giant Cell Chronic Arteritis.—Gilmour cites 4 cases of a rare and little known form of arteritis which affects the aorta, the branches of the aortic arch and their branches and possibly other arteries. Syphilis was excluded in 3 of his cases and in most of those reported in the literature. Tuberculosis also may be excluded. The essential microscopic change was inflammation, and the prodromal symptoms were strongly suggestive of infection. The microscopic and clinical features do not resemble those in other types of arteritis. It is probable that the disease is a separate entity. In the branches of the arch of the aorta and in the internal and external carotid arteries the distribution of the disease is focal, bilateral and symmetrical, while in the aorta it is usually widespread. The inflammation apparently heals in time, but death has occurred from rupture of an aneurysm or from thrombosis during active inflammation. Multinuclear giant cells were present in most of the affected vessels, therefore the name giant cell chronic arteritis.

Lancet, London

2:415-442 (Oct. 11) 1941

Cysticercosis of Brain with Epilepsy and Papilledema. W. E. C. Dickson and J. D. Willis.—p. 415.

Silicosis in Stourbridge Fireclay Miners. S. Deaner.—p. 417.

Syphilis of Lungs: Case. A. Clark.—p. 420.

*Action of Bismuth Carbonate in Gastric Disease. S. Alstead.—p. 420.

*Blast Injury of Lungs. J. N. O'Reilly and S. R. Gloyne.—p. 423.

Action of Bismuth Carbonate in Gastric Disease.—Alstead tried to determine the value of bismuth carbonate in relieving the pain of gastroduodenal disease and the fate of the salt in the stomach. His in vitro and in vivo experiments do not suggest that therapeutic doses of bismuth carbonate protect the gastric mucosa. After administration the salt collects in the most dependent part of the stomach and tends to adhere to a small area of the mucous membrane in the prepyloric region. The ulcer-bearing area of the stomach is rarely affected. Bismuth carbonate may exert an astringent action on the empty stomach, but even under favorable conditions this action is slight. In practice it must be considered negligible because of the minute amount of bismuth in solution with the mucoprotein of gastric juice. When a gastric astringent is required tannic acid, in the form of glycerin of tannic acid, is more reliable. The antacid effect of therapeutic doses of bismuth carbonate is trivial or entirely absent. Although large doses produce appreciable changes in gastric acidity, the changes are transient, and the side effects of such quantities, especially constipation, cannot be disregarded. In gastroduodenal disease bismuth carbonate is no more valuable than powdered milk or lactose in relieving pain.

Blast Injury of Lungs.—O'Reilly and Gloyne present 17 cases of pulmonary injury from the blast of high explosives. None of the 17 men injured were buried under débris. Shock was profound in 5 and was definite though not dangerous in the others. Dyspnea was a constant feature. Dyspnea continued till death in the 4 patients who died. Cyanosis was a common feature. Two types of pain were complained of—a central deep constant and especially severe pain and a less severe more lateral pain made worse by deep breathing. The less severely injured patients stated that the lateral pain was preventing them from breathing. The central pain disappeared after a few days in the patients who recovered, while the other pain remained for at least a week. Pain in the abdomen was common. At necropsy in each of the 4 cases extrapleural hemorrhages were observed. The intercostal spaces appeared black in contrast to the white bands of the ribs. The hemorrhages may have irritated the intercostal nerves, causing rigidity of the abdominal wall, or damage to the abdominal muscles may have caused the rigidity. A laparotomy should not be performed unless specifically indicated. Free hemoptysis was observed in 2 patients and in the others blood-stained sputum and brightly stained froth in the air passages. A number had a cough after the first twenty-four hours, in some of them troublesome. In patients with uncomplicated injury the cough and sputum disappeared in ten days, but it persisted in those with severe late effects or complications. Restlessness was a constant symptom and bore a direct relation to the severity of the damage. The pathologic observations suggest that the restlessness is due to an irritative cranial lesion. Ruptured eardrums were noted. Purulent otorrhea developed in some patients, and in a few it was extremely resistant to treatment. Roentgenograms of the chest of 7 patients were taken within seventy-two hours of injury. In those with severe injury there was a heavy mottling over large areas of the pulmonary fields. The most striking pathologic feature was an effusion of blood. The chief microscopic characteristics were an extensive outpouring of erythrocytes, the rupture of elastic tissue and capillaries, secondary infection with streptococci and bronchopneumonia. All patients with shock were treated with heat and morphine. Seven patients were given oxygen continuously, and transfusions of blood and/or plasma were given to 5. Unless concomitant hemorrhage exists plasma is indicated. Sulfapyridine was given prophylactically to 5 patients, and when pneumonia developed the dose was increased. The drug was withdrawn when the temperature dropped to normal. In blast injury of the lung rest, which was possible only with morphine, is of prime importance and anesthetics are contraindicated.

Chinese Medical Journal, Peking

60:99-200 (Aug.) 1941

*Treatment of Infantile Tetany with Dihydrotachysterol (A. T. 10). Theresa T. Woo, C. Fan and F.-T Chu.—p. 99
Hemolytic Streptococci from Parturient Women, with Reference to Their Serologic Classification and Relation to Puerperal Fever. C. J. Wu.—p. 109.
Increased Resistance to Syphilis in Rabbit Following Bilateral Orchidectomy. C. K. Hu and S. N. Tsao.—p. 118.
Comparative Study of Four Slide Precipitation Tests for Syphilis. E. C. J. Sung.—p. 126.
Study of Outbreak of Scurvy: I. Clinical Features. Julia Morgan and A. S. Gault.—p. 141.
Management of Bilateral Advanced Pulmonary Tuberculosis: Report of Clinical Results of 100 Cases of Simultaneous Bilateral Artificial Pneumothorax and Twenty-Five Cases of Contralateral Pneumothorax Combined with Thoracoplasty. M. H. Chien.—p. 156.
Diagnosis of Tuberculosis of Mandible. C. M. Meng.—p. 169.
Determination of Soybean Milk Used as an Adulteration in Cow's Milk. F. Liebenthal and W. H. Adolph.—p. 174.
Peculiar Morphology of Malaria Parasite from a Patient and Possibility of Its Being Plasmodium Ovale. Y. T. Yao and C. C. Wu.—p. 178.
Preoperative Improvement with Tourniquet. P. E. Adolph.—p. 184.
Abscess of Sclera. E. Chan.—p. 189.

Dihydrotachysterol for Infantile Tetany.—Woo and her co-workers gave dihydrotachysterol to 5 Chinese infants (from 4 to 52 days old) suffering from infantile tetany. The pathogenesis of the tetany of these infants probably was a congenital lack of vitamin D and calcium. The diets of 4 of the mothers were deficient in vitamin D or calcium or both. The roentgenograms of 3 infants presented evidence of coexisting rickets. Dihydrotachysterol was highly effective in controlling the tetany in 4 infants. Its effect on the concentration of serum calcium and phosphorus was prompt. After therapy the coexisting rickets of 2 infants showed roentgenologic improvement. Fairly large doses, 1 to 1.5 cc. daily, of dihydrotachysterol for one to four days were necessary to raise the serum calcium to a normal level. Therapy with the drug must be individualized. It is imperative that the blood calcium level be determined at intervals before and after treatment is instituted. The chief advantage of dihydrotachysterol to vitamin D and calcium in the treatment of infantile tetany appears to be its prompt action; the principal objections are its high cost and the danger of hypercalcemia if excessive doses are used.

Schweizerische medizinische Wochenschrift, Basel

71:1009-1036 (Aug. 30) 1941. **Partial Index**

Anorexia Mentalis and Simmonds' Disease. M. Roch and Marcel Monnier.—p. 1009.
*Antihormones. C. A. Joël.—p. 1011.
Circulatory Collapse, Temporary Anuria and Extrarenal Azotemia. O. Spühler and H. U. Zollinger.—p. 1013.
Mineral Metabolism. A. Ulrich.—p. 1020.
Indications for Transfusion of Universal Preserved Blood. R. Fischer.—p. 1024.

Antihormones.—Joël discusses some properties and the clinical importance of the antigonadotropic and of the antithyrotropic substances. The antigonadotropic substance cannot be completely purified but remains associated with the serum globulins. It does not develop in a special organ, but rather in the serum and probably in the reticuloendothelial system. Analysis of pregnancy serums revealed that antihormones are not formed during pregnancy. From this it was concluded that normally the body does not employ antihormones as regulatory devices and that it reacts with antihormone formation only if heterogenic hormones are administered. The antithyrotropic substances are found in the spleen and in the liver of animals treated with thyrotropic substances. Antithyrotropic hormone occurs in normal serum, whereas the antigonadotropic factor is not present in the serum of untreated animals. Antithyrotropic substance occurs in various disorders. In patients with exophthalmic goiter, for instance, it is present in smaller quantities than in healthy persons, whereas in cretins it occurs in larger quantities. The author raises the question whether antihormone formation plays a part in prolonged hormone therapy. Insulin, epinephrine, solution of parathyroid, vasopressin, oxytocin, estrone, thyroglobulin and thyroxine do not cause habituation, but it is generally admitted that habituation is produced by the anterior pituitary hormones that contain protein, that is, gonadotropic, thyrotropic, contrainsular and other hypophysial hormones. However, the clinician needs to fear the antihormone formation with these latter hormones only, if he injects them daily for periods of months. Gonadotropic substance of human origin (substance prepared from pregnancy urine) does not lead to antihormone formation; however, extracts of mare urine do so, if they are given daily for three months or more. The author thinks that antihormone formation can be avoided by alternating the preparations.

71:1037-1060 (Sept. 6) 1941. **Partial Index**

Results of Etiologic Research on Goiter During Sixty Year Period from 1880 to 1940: Significance for Prevention. F. Wolter.—p. 1037.
*Tolerance for Large Doses of Anhydrohydroxyprogesterone After Hysterectomy and Castration and Conditions of Elimination. R. Wenner and C. A. Joël.—p. 1040.
Steroids Eliminated in Urine During Administration of Anhydrooxyprogesterone. M. W. Goldberg and E. Hardegger.—p. 1041.
*Iodine Distribution in Normal and Sclerotic Vascular Walls. P. Masson.—p. 1042.

Anhydrohydroxyprogesterone After Hysterectomy and Castration.—The investigations of Wenner and Joël were made on 2 women of 38 and 40 respectively who had undergone total hysterectomy twenty-eight and thirty days before the administration of the hormone. The ovarian function had been excluded by massive doses of roentgen rays that are used in single carcinoma irradiations. However, the time interval between roentgen castration and hormone administration was relatively short, seven and eight days, respectively. It is of clinical interest that 1 Gm. of anhydrohydroxyprogesterone, given on three successive days, was well tolerated. Chemical analysis of the urine corroborated Frank's observation that no pregnandiol is eliminated after the administration of anhydrooxyprogesterone. Two other factors that were detected seem of special interest: 1. The control urine as well as the urine collected after the treatment contained from 0.1 to 0.2 mg. of pregnandiol per liter. This corresponds to the observation made by Jones and Te Linde that hysterectomized women eliminate pregnandiol without the administration of progesterone. From this it must be concluded that it is formed in the body without cooperation of the uterus and even eight days after exclusion of the ovaries. 2. The control urine and the urine collected after treatment contained also approximately 0.2 mg. of androsterone per liter. Thus the formation of androsterone and pregnandiol in the female organism is not dependent on the uterus and probably not on the ovaries. The authors think that in the search for the site of formation the adrenal cortex should be considered, because it plays an important part in the stearin metabolism.

Iodine Distribution in Vascular Wall.—Masson used rabbits for his experiments, because arteriosclerosis can readily be produced in them. Of 6 rabbits which were free from arteriosclerosis 5 were given potassium iodide and 1 was not. In 3 the aorta was free from iodine; in the 3 others only small quantities of iodine were detectable. In the aortas of the animals which had been made arteriosclerotic with cholesterol and had been treated with potassium iodide, it was always possible to demonstrate iodine, and except for the iodine content in 1 animal, the iodine content was always greater than in the nonsclerotic animals. The author concludes from these observations that iodine proves so valuable in arteriosclerosis because the vascular wall as such has a certain affinity for it but that the iodine affinity of the arteriosclerotic wall is especially great. With regard to iodine affinity, the sclerotic vascular tissue behaves like the syphilitic and the tuberculous tissue.

Brasil-Medico, Rio de Janeiro

55:625-640 (Sept. 13) 1941. **Partial Index**

*Therapy of Tropical Ulcer with 1 per Cent Potassium Arsenite Solution (Fowler's Solution). C. de Castro.—p. 625.

Potassium Arsenite Solution for Tropical Ulcer.—De Castro reports good results in 150 cases of tropical ulcer from the following therapy: The ulcer is thoroughly cleaned with pieces of cotton or of gauze. Scrapings of the tissues at the bottom of the clean ulcer are taken for smears. A swab of absorbent cotton is soaked in a 1 per cent potassium arsenite solution (Fowler's solution) and introduced into the ulcer in

such a manner as to have it in constant contact with all the excavations, bottom and borders of the ulcer for ten minutes. Then it is removed and replaced by a piece of plain gauze and the treatment repeated every day up to the disappearance of spirilla in the smears, which, as a rule, takes place in four days and coincides with diminution of the secretion and cleaning of the ulcer. At this point the application of potassium arsenite is stopped and replaced by application of an ointment which is prepared with petrolatum, yellow mercuric oxide, zinc oxide and hydrous wool fat. Complete healing is obtained in about one month. The scars are fine, flexible and smooth. The treatment is moderately painful, but it is well tolerated. For children and for persons sensitive to pain it is advisable to induce a light superficial imbibition anesthesia with 2 per cent procaine hydrochloride immediately after cleaning the ulcer and before applying the potassium arsenite solution. The therapy can be given to ambulant patients. It is practical, economical, harmless and reliable. Early in its course the necrotic tissues of the ulcer are eliminated, the secretion is favorably modified, the bad odor of the ulcer is controlled and the ulcer is sterilized.

Pasteur, Revista Mensual de Medicina, Mexico, D. F.

2:57-88 (Sept. 15) 1941. **Partial Index**

Sulfanilamide Therapy in Gastrointestinal Diseases. W. Nimeh.—p. 57.
*Sulfanilamide in Therapy of Chancroid. L. G. Vazquez Vega.—p. 70.

Sulfanilamide for Chancroid.—Vazquez Vega reports good results from sulfanilamide therapy for chancroid, alone or complicated by acute suppurative adenitis, for chancroid phymosis and for phagedenic chancroid. The drug may be given either locally, in the form of powder, or by mouth. When the local treatment is used the entire chancroid or adenitic lesion is covered with sufanilamide powder (which is obtained by pulverizing sulfanilamide tablets) and dressed with plain gauze; the treatment is changed every day or every other day until healing of the chancroidal lesion. In cases of chancroid phimosis a 25 per cent suspension of the drug in petrolatum is prepared, and a swab of cotton is soaked in the preparation and brought into contact with the lesion. The duration of the local treatment depends on the clinical reaction. Generally the patient is cured in two weeks. The treatment is harmless and efficacious and may be given to ambulant patients.

Revista Clínica Española, Madrid

3:89-188 (Aug.) 1941. **Partial Index**

Chemical Composition of Bone and Biochemistry of Ossification. J. Ruiz Gijón.—p. 89.
Exploration of Terminal Ileum. C. Marina Fiol and J. Rof Carballo.—p. 97.
Clinical and Experimental Study of Exanthematous Typhus: Epidemic in Sevilla. G. Romero Escacena, J. Bolinches and M. Álvarez.—p. 106.
Study of the Fourth Derivation of the Electrocardiogram. J. Lozano López.—p. 115.
Luxation of Long Part of Biceps. J. Díaz de Rábago and F. López Areal.—p. 119.
Spasmus Nutans and Salaam Spasm. M. Calzada Rodríguez.—p. 125.
Consideration of Two Cases of Spurious Arterial Aneurysms, One of Them with Arteriovenous Fistula. J. Gascó Pascual and C. Carbonell Antoli.—p. 131.
*Functional Test of Stomach. R. Chamorro-R. Salinas.—p. 139.

Test for Gastric Cancer.—Chamorro-R. Salinas explores and evacuates the fasting stomach by means of Einhorn's tube. He then introduces 250 cc. of a 5 per cent alcoholic solution to which several drops of a 1 per cent solution of methylene blue have been added. After that he aspirates every fifteen minutes specimens of fluid showing a homogeneous blue. The intensity of the coloration gradually subsides until it has completely disappeared. Normally the coloration persists for twenty-four hours and more and is independent of the gastric acidity. However, the author states that in the presence of gastric cancer, and gastric cancer only, an ascending discoloration can be observed in the test tubes; at the end of an hour they are completely colorless, or at the most they show a blue ring at the upper rim. This metachromatic discoloration has no connection with anacidity, the presence of organic acids or blood, and the author regards it as specific for gastric cancer.

Archiv für Kreislaufforschung, Dresden

9:1-122 (July) 1941. **Partial Index**

Influence of Exclusion of Vagus on Blood Pressure. A. Jarisch.—p. 1.
*Electrocardiographic Investigations During Electric Shock Therapy of Schizophrenia. M. Streit.—p. 11.
Estimation of Pulmonary Circulatory Disturbances. K. Hohenner.—p. 45.
Scarlet Fever Myocarditis. J. Eckert-Möbius.—p. 91.

Electrocardiographic Investigations During Electric Shock.—Streit describes electrocardiographic studies on 39 schizophrenic patients who underwent electric shock therapy. In all, one hundred and ninety electrocardiograms were made after thirty-five total shocks and thirty abortive shocks. The changes after total shock are mostly disturbances in the rhythm. At first there is usually a sinus tachycardia up to 250 beats per minute. After this has subsided, various types of arrhythmia appear (sinus arrhythmia, auricular and ventricular extrasystoles, combinations of auricular and ventricular extrasystoles with vagus arrhythmia). The T wave is elevated immediately after the attack, but three to eight minutes later it passes through a phase of flattening. At the end of one to two hours the changes disappear. The ST interval is lowered in approximately 25 per cent of the cases. This lowering of the interval often accompanies an elevation of the T peak. Of two electrocardiographic recordings made during the latent period one shows, in addition to a sinus tachycardia, an elevation of the T wave and the second a slight flattening of the T wave. During the abortive shock, rhythmic disturbances are rare; auricular and ventricular extrasystoles were observed in 3 cases. The abortive shock is characterized by severe bradycardia and cardiac arrests. The irregularities in the heart beat are the most important of the electrocardiographic changes during electric shock. Immediately after the attack, the irritation of the sympathetic, with sinus tachycardia, predominate; some minutes later, vagus effects become evident, in that now there are also a sinus and vagus arrhythmia and auricular, and somewhat less often ventricular, extrasystoles. Generally, the extrasystoles disappear after four or five minutes. The many extrasystoles after electric shock were a surprise, since Bini and Cerletti, the investigators who developed the electric shock therapy, observed only mild arrhythmias with extrasystoles and considered them insignificant. Streit's observations indicate that the electrocardiographic aspects of electric shock are similar to those of metrazol shock. The electric shock therapy is not without danger for the circulation. The cardiac arrests may, under certain conditions, lead to permanent heart failure and the frequent rhythmic disturbances to ventricular fibrillation.

Deutsche medizinische Wochenschrift, Leipzig

67:723-830 (July 4) 1941. **Partial Index**

Experiences with Local Chemotherapy with Mesudin-Prontalbin. E. Schneider.—p. 723.
*Clinical Observations on Pellagra and Its Treatment with Nicotinic Acid Amide. H. Schroeder and Dramoff.—p. 726.
Diagnosis and Therapy of Chronic Poisoning with Arsenic. A. Hámori.—p. 728.
Anatomic Aspects of Fatal Infections with Paratyphoid Breslau Bacilli. H. Meessen and H. H. Merkel.—p. 731.
Clinical Experiences with Depot Insulin. R. Schwab.—p. 738.
Tincture of Belladonna in Gastrointestinal Disturbances. R. F. Weiss.—p. 738.

Treatment of Pellagra with Nicotinic Acid Amide.—Schroeder and Dramoff state that pellagra in Bulgaria occurs endemically in regions in which maize and wheat grits are the only sources of protein in the diet. These vegetable proteins require the pellagra preventive substance for their proper utilization; that is, the intake of large quantities of maize or wheat grits increases the requirements for the antipellagra factor. The toxic action of vegetable proteins is often accompanied by porphyrinuria. This disorder is a constant symptom of pellagra, and it is encountered also in favism (bean poisoning) or in lathyrism. Porphyrinuria causes light-sensitivity of the skin of pellagrins. The treatment of pellagra has been greatly simplified since the discovery of the pellagra preventive substance. However, it should be remembered that pellagra is rarely a monoavitaminosis. The pellagrous manifestations of the gastrointestinal tract, of the skin and of the nervous system yield rapidly to treatment with nicotinic acid, but the general weak-

ness and anemia require the simultaneous administration of the other factors of the B complex in the form of yeast or liver extract. In order to insure a permanent cure of pellagra it is necessary to change the diet or to administer the entire B complex. The daily dose of nicotinic acid or of nicotinic acid amide is between 100 and 1,000 mg. It has proved advantageous to give 60 to 125 mg. four times daily by mouth. Beef, pork, rabbit meat, hog liver, milk, Savoy cabbage and yeast are rich natural sources of the pellagra preventive substance.

Deutsche Zeitschrift für Chirurgie, Berlin

254:289-406 (Jan. 4) 1941. **Partial Index**

Appendicitis and Its Treatment. J. Jungbluth.—p. 289.
Clinico-Anatomic Correlations in Exophthalmic Goiter. G. Guerreri d'Antona.—p. 318.
*Anuria After Transfusion of Conserved Blood. W. Brunner.—p. 350.
Desirability of More Extensive Use of Choledochoduodenostomia Externa. H. Geissendörfer.—p. 379.

Anuria After Transfusion of Conserved Blood.—Brunner says that at his clinic the transfusion of conserved blood produced practically the same results but also the same complications as did the transfusion of fresh blood. Rarely he saw more severe reactions after the transfusion of conserved than after the use of fresh blood. He thinks that a final evaluation is still impossible, since numerous investigations are still uncompleted. He does not share the view expressed by Jeanneney and his collaborators, according to which the danger of transfusion shock is less after the transfusion of conserved blood than after the transfusion of fresh blood, because the colloidal state of conserved blood is already stabilized and its composition can be better controlled. The author warns against too great optimism in this respect and reports 3 cases in which anuria resulted following the transfusion of conserved blood. Blood transfusion was indicated on account of shock. All recipients had blood of group O, and so did the donors, with one exception, when homogenized blood was used from four donors with group O blood and one donor with group A blood. The transfusion, which in each case provided 300 cc. of blood, was given, with additional physiologic solution of sodium chloride, in the form of an intravenous drip lasting for two or three hours. The preliminary biologic tests never disclosed disturbances, and there were no reactions during the transfusion. The ages of the conserved bloods varied from eleven to thirty-two days, but in the first patient, even the eleven day old blood produced a thirty-six hour anuria with subicterus as the result of massive hemolysis. It is possible that an accidental unilateral ureteral ligature contributed to the anuria, which, however, was first elicited by the hemolysis. Subsequently there developed a refractory renal insufficiency with dynamic ileus without peritonitis. In the second case, of the most severe anuria, the course terminated in death five days after the transfusion of conserved blood, because the anuria failed to respond to alkali therapy, to diuretics, to vasodilator agents or to lumbar anesthesia. Renal decapsulation or denervation was impossible on account of the greatly impaired general condition. In the third case, in which the homogenized conserved blood was used, the course was the same as in the 2 others. Following anuria of thirty-six hours' duration, renal insufficiency developed which seventeen days later terminated in death from uremia.

254:407-554 (April 15) 1941. **Partial Index**

Roentgenologic Examination of Neck and Head of Femur. O. Voss.—p. 407.
Clinicotherapeutic Experiences in Echinococcosis of Spleen. A. Nanna and E. Adam.—p. 422.
Partial Inversion of Duodenum. G. Töndury.—p. 442.
*Anaphylactic Reaction After Electroresection of Prostate. F. Arnholdt.—p. 460.
Endangiitis Obliterans of Brain. P. Sunder-Plassmann.—p. 463.
Clinical and Experimental Investigations on Regeneration Capacity in Epiphysial Zone of Long Tubular Bones. F. Becker.—p. 488.
Treatment of Acute Osteomyelitis. K. Kratochwil.—p. 542.

Anaphylactic Reaction After Electroresection of Prostate.—Arnholdt reports on a man aged 76 with hypertrophy of the prostate complicated by considerable renal damage and mild urinary infection. Electroresection was carried out with the aid of local anesthesia, after two weeks of preliminary treatment. The prostate had no median lobe, but the two lateral ones, particularly the right one, considerably constricted the urethral lumen. About 3 Gm. of tissue in all was resected from the two lobes. Moderate hemorrhage was readily arrested, and a catheter was introduced. The postoperative course was uneventful, but the result was unsatisfactory in that the residual urine still amounted to 170 cc. After thirty-three days, the electroresection was repeated, the removed prostatic tissue again amounting to 3 Gm. Three to four hours after the second electroresection there appeared, along with a sensation of extreme heat and itching, erythema and swelling of skin, particularly on the face and the extremities. The patient was given, immediately and on the following days, intravenous injections of 10 cc. of calcium-Sandoz. The cutaneous manifestations and the temperature increased on the following day and reached their maximum in the afternoon. The swelling and the exanthem involved the entire body but were especially severe on the face. Respiration was accelerated, and the pulse was soft and frequent. There were severe head and muscular aches and itching and burning of the eyes. With desquamation of the skin, the symptoms gradually subsided in the course of three days. The exanthem resembled a severe urticaria. The clinical picture indicated a toxic or allergic genesis. The patient had received only the medicaments he had been given before and had eaten nothing but the customary breakfast. The author concludes that the anaphylactic reaction was caused by the combustion products of the electroresection, pointing out that the electric current denatures the homogeneous cell protein into a heterogeneous substance, which sensitized the body during the first electroresection; that is, in the course of days the patient became allergic and the renewed electroresection elicited the anaphylactic reaction.

Nordisk Medicin, Stockholm

11:2577-2666 (Sept. 13) 1941

Hospitalstidende

Lack of Antipernicious-Anemia Principle in Liver Extract from Electively Resected Fundus of Stomach of Swine. (Clinical-Therapeutic Investigation.) S. Petri, J. Bing, E. Nielsen and Aage Kjerbye Nielsen.—p. 2577.
Determination of Vitamin B_1 Content in Urine: Modification of Thiochrome Method. K. Wassmann.—p. 2582.
Recent Investigations on Coagulation of Blood. T. Astrup.—p. 2586.

Finska Läkaresällskapets Handlingar

Adjustment of Aged to Life and Their Struggle Against Death. E. Quarnström.—p. 2591.
Reaction in Rectum After Irradiation Treatment of Cancer of Uterus. J. J. Chydenius.—p. 2595.
Changes in Size and Form of Red Blood Corpuscles in Infants Shortly After Birth. C. A. Hernberg.—p. 2599.
*Secretion of Gonadotropic Hormones in Urine in Cases of Tumor of Testis. L. Furuhjelm.—p. 2603.
Amyloidosis in Chronic, Not Suppurative Affections of Joints. R. Gordin.—p. 2609.

Gonadotropic Substance in Urine in Tumor of Testis.—Furuhjelm studied 44 cases of malignant tumor of the testis and 1 of extragenital tumor that produced gonadotropic substance. There were 21 cases of other lesions of the testis and 69 other cases of different diseases in men as controls. He found the secretion of gonadotropic substance in the urine an aid in diagnosis in cases of tumor of the testis. However, increased secretion of gonadotropic substance also occurs in certain other diseases in men, and the biologic percentage of error must be considered. He states that in hormone analysis qualitative hormone differentiation according to Hamburger is of great value. If chorionic gonadotropin is secreted, mixed epithelioma is most likely. If in addition the pregnancy reaction is positive, chorioepithelioma can be suspected. If the follicle stimulating factor is established in increased amounts, a seminoma is indicated. Even if it does not agree with the histologic diagnosis, hormone analysis may be decisive for therapy and prognosis. Tumors of the testis which secrete chorionic gonadotropin usually have only a transient radiosensitivity, while those which secrete the follicle stimulating factor are often more sensitive to roentgen treatment. The prognosis is most favorable in the cases in which less than 165 mouse units of the follicle stimulating factor is secreted. It is especially unfavorable if both kinds of gonadotropic substance are established.

Hygiea

Vaccination Against Infectious Diseases as Measure of Public Protection. C. Kling.—p. 2613.

Book Notices

The Treatment of Infantile Paralysis in the Acute Stage. By Elizabeth Kenny. Cloth. Price, $3.50. Pp. 285, with 72 illustrations. Minneapolis & St. Paul: Bruce Publishing Company, 1941.

This book represents an attempt to present the argument that spasm is the damaging and ever present symptom of the disease infantile paralysis. Miss Kenny describes in infinite detail the treatment of infantile paralysis in the acute stage by means of hot wet compresses without splints or braces. The terminology used is somewhat confusing. Any physician who has been thoroughly grounded in physiology, anatomy and pathology and has observed the degenerative changes in the anterior horn cells of the spinal cord of a monkey or of a human victim of acute anterior poliomyelitis will find much in the Kenny theory that is absurd and unscientific. The confusing discussion of pathologic principles and the rather odd mixture of anatomic terms and descriptions make it difficult to read the book or to follow some of the arguments by the author.

Spasm is often present in the early stages of acute anterior poliomyelitis and as such has been seen by every one who has studied the disease. Miss Kenny has definitely shown that the early application of hot wet dressings properly applied will aid in the reduction of the amount of muscle spasm, in the relief of pain and in the recovery of the patient. On the other hand, she has failed to recognize that fibrous tissue replacements of muscles, subsequently producing shortening and actual contracture, are not spasm. The enthusiasm of this remarkable woman is shown in every chapter of the book. This enthusiasm borders on religious fanaticism. Also she is completely on the defensive. In this book she has described her early experiences in Australia and England and the more recent and perhaps more pleasant years in Minneapolis.

The Kenny opposition to the use of splints is undoubtedly engendered by the fact that she has seen a great many patients with joints stiff and muscles fibrosed by unwise, prolonged, total immobilization. To this extent her argument is well taken. However, there are patients for whom certain types of splints are important even during the acute or subacute stages of the disease. There are patients who would undoubtedly die of respiratory paralysis if they were not placed in a respirator. There are other patients who would never walk a step without the aid of the braces which she condemns.

The medical profession of the world owes to Sister Kenny a debt of gratitude for having made us realize that prolonged splinting without exercise, without heat and moisture applied to the limbs, is harmful. It is hoped, however, that the public and the medical profession in general will not be so completely swayed by the enthusiasm of this remarkable woman that they will refuse to use splints where only splints can prevent deformities or will refuse braces when only through braces can independent and self care be made possible. We should be sufficiently liberal minded to accept the good elements of the Kenny theory without losing our balance and falling head over heels into a pit which both Galen and Hippocrates succeeded in climbing out of many centuries ago.

Surgery of the Heart. By E. S. J. King, M.D., M.S., D.Sc. Cloth. Price, $13.50. Pp. 728, with 268 illustrations. Baltimore: William Wood & Company, 1941.

The author is honorary surgeon to outpatients, Royal Melbourne Hospital of Melbourne, Australia. The book originated as a dissertation prepared by the author and submitted to the Royal College of Surgeons in 1938. It was awarded the Jacksonian Prize. The book is divided into two sections. The chapters in the first section are on the development of the heart, comparative anatomy of the heart, the anatomy of the heart, developmental abnormalities of the heart, histology of the heart, physiology of the heart, pathology of the heart, radiology in examination of the heart and electrocardiography. The chapters in the second section are on the surgical approach to heart diseases, experimental investigations, diseases of the heart, diseases of the myocardium, diseases of the coronary vessels, diseases of the endocardium, diseases of the pericardium, diseases of the great vessels, diseases of the pulmonary artery, diseases of the pulmonary veins, diseases of the aorta and diseases of the venae cavae.

The book is more than a surgical treatise. A large part is devoted to nonsurgical subjects. The author is thorough in his review of the literature. This is the most valuable feature of the book. Any one desiring a bibliography will find it readily available.

The literature on the surgery of the heart presents difficulties in the way of analysis. The total number of operations on the heart is not large when compared to operations on other organs, and the experiences of any one surgeon are relatively few. This lack of broad experience results in a paucity of data on the subject. The surgical experiences are inadequate to give a final answer to many questions. We deal then with the expression of opinions and some of these are of a conflicting nature. The author does almost as well as can be expected with material of this nature. For example, he advocates opening the pericardium in patients with enlarged heart. After advocating this operation he concludes that "the indications for the procedure are not yet known; a great deal of information is required before they can be determined exactly. On the other hand, the operation may be performed readily under local anesthesia and without appreciable risk. For this reason the specification of rigid criteria is not, in the early stages of investigation, so important as it is for technically formidable procedures." After reading the discussion of this subject, the reader cannot be certain whether this operation should be applied. If it is as good as the author claims it to be, why has the operation not been done more frequently so that the indications are clearly known? It is obvious that additional critical experiences are necessary to ripen this subject. Similar statements can be made about other subjects discussed in the book. The reviewer doubts whether heart surgery is far enough developed for a book.

Cancer of the Face and Mouth: Diagnosis, Treatment, Surgical Repair. By Vilray P. Blair, M.D., Sherwood Moore, M.D., and Louis T. Byars, M.D. Cloth. Price, $10. Pp. 599, with 324 illustrations. St. Louis: C. V. Mosby Company, 1941.

This is a new and important study of an old and extremely important subject. Washington University and its associated hospitals in St. Louis have afforded the "terrain" on which these three authors, working as a team, carried out intensive studies on epithelial cancer in 1,500 cases over a period of twenty years. A foreword by Dr. J. M. T. Finney sets forth the "right" of these men to authoritative consideration.

One would assume that external malignant growths afford the best chance for early diagnosis. Not so here. Only from 5 to 10 per cent of all cases can be classified as "early." Three reasons are cited: 1. The patient refuses the diagnosis or accepts it and demands a guaranteed cure. Most often he becomes the victim of quackery and returns too late to his first adviser. 2. There is a lack of diagnostic acumen when diagnosis might have been made early. 3. Misinterpretation occurs of the microscopic report of the pathologist who writes "no cancer found," which is not at all understood by the practitioner when he assumes that this means no cancer present. Moreover, one is likely to regard cancer of the mouth or face as "mild," but some of these growths are terribly malignant from the outset, notably cancer of the sinuses, "usually of the highest grade of malignancy." The diagnostician must depend on his eye, his finger, the knife and the microscope. When all of these are given their true weight, the patient's chances of life extension are multiplied many times.

One concludes from this book that the authors believe surgery the method of choice in this field. Irradiation holds second place save in those advanced cases in which surgery seems impossible. But at operation the surgeon must avoid "grafting" spilled cancer cells into a fresh wound, and he must not "squeeze" these cells into the general blood and lymph circulation.

These principles are so axiomatic that they are probably overlooked now and then. In any event the salvation of the patient depends on early diagnosis, prompt, effective treatment, selection of the correct treatment for the individual case and persistent execution of "the plan" originally set down.

Chapter XVIII, written by Dr. Sherwood Moore, deals with irradiation; that is, with the use of roentgen rays, radium or

radon, singly or in combination or in sequence. While these agents may be extremely useful, especially in making cancer more "tolerable," they can cause a fatality. It is difficult to control them completely; they act on normal cells adversely as well as on diseased cells. In the general body economy they may cause acidosis or, at least, increase it and may bring about "roentgen sickness," the symptoms of which are anorexia, general malaise, nausea, sometimes vomiting and, if treatment extends over the abdomen, intractable diarrhea. Under such conditions the situation gets entirely out of hand, and the patient hurries to his doom.

While there are no colored plates in the book, the multiplicity of excellent photographs and the prodigality with which line drawings have been showered on the pages in order that the reader may thoroughly understand operative technic, plus the quality of paper and print, make this volume first in its field, and one may predict its usefulness over a long span of years to come.

Diseases of the Blood and Atlas of Hematology with Clinical and Hematologic Descriptions of the Blood Diseases Including a Section on Technic and Terminology. By Roy R. Kracke, M.D., Professor of Bacteriology, Pathology and Laboratory Diagnosis, Emory University School of Medicine, Atlanta. Second edition. Cloth. Price, $15. Pp. 692, with 100 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1941.

The second edition of this excellent book has been enlarged by the addition of one hundred and sixty pages, ten new color plates and twenty-nine other new illustrations. Among the new material are data on the fractionation of liver extract, new chapters on hemolytic anemias and hemoglobinuria, new material on the action of drugs on the blood, hemoglobin and its derivatives, transfusion and the operation of a blood bank, the use of blood plasma and recent work on the bone marrow. There is a section on vitamin K and new material on the treatment of leukemia. The plates and pictures are unusually good, and the text is presented in a clear cut fashion with the free use of outlines and specific definitions. The section on the blood in animals will be welcomed by many experimenters. The chapter on hematologic technic is extensive and detailed. The bibliography has been brought up to date and the index is extensive. The book is now well established as one of the classics of hematology and is indispensable for any one looking for authoritative, comprehensive and well ordered data on blood.

The Microbe's Challenge. By Frederick Eberson, Ph.D., M.D., Director of Laboratories; Pathologist, Gallinger Hospital, Washington, D. C. Cloth. Price, $3.50. Pp. 354, with portrait. Lancaster, Pa.: Jaques Cattell Press, 1941.

For the reader who wants detailed and technical information about bacteria translated into terms understandable for the layman, this is an excellent, if difficult, book. The book is as clear an explanation of highly technical relationships as could be expected, in view of the difficulties of translating specialized scientific materials into language readily understood by the nonprofessional reader. The book contains chapters on the fundamental facts relating to bacteria in general, the historical background of our knowledge of bacteriology, the ways of parasites, changes and variations in microbe life, the chemical behavior characteristics of bacteria, vaccines and viruses and insect borne diseases. Research and a survey of the situation today are each made the subject of a chapter. The book is exceptionally well made and beautifully printed with a clear type face generously leaded. Its only illustrations are a frontispiece photograph of Louis Pasteur, an insert page showing the first microscope on one side and van Leeuwenhoek on the other, an occasional drawing after the manner of woodcuts and a map showing distribution of plague in Manchuria in 1910. There is an adequate glossary and a satisfactory index.

The Complete Weight Reducer. By C. J. Gerling. Cloth. Price, $3. Pp. 246. New York: Harvest House, 1941.

The title—and some of the subtitles on the slip cover: "The Modern Spot Reducer," "Manual of Slimming Garments"—filled the reviewer with apprehension, which however was largely relieved after reading the text. The book is written for the "average reducer," i. e. for the interested layman, and may be used as a dictionary, the various points of interest being listed in alphabetical order. It has practical merit mainly in describing and exposing most of the popular quackeries and frauds and in stressing the dangers of self prescription as well as the necessity of medical consultation. In its more ambitious aims—when it tries to explain metabolic processes, the role of endocrine glands, the importance of heredity—it is less successful, as such points do not lend themselves to categorical, lexicographic presentation. Altogether, the book should be popular with those "reducers" who want some information on their problems even though it is not always truly instructive and in some instances (effect of exercise on local fat deposits) inaccurate.

Die Grösse und Form der roten Blutkörperchen bei Menschen verschiedenen Alters unter physiologischen Verhältnissen. Von Carl August Hernberg. Acta medica Scandinavica, Supplementum CXXII. Paper. Pp. 92, with 21 illustrations. Helsingfors: Mercators Tryckeri, 1941.

This monograph presents a comprehensive review of the literature and an anlysis of the blood of 236 persons studied by the author. The data are divided in seven age groups: infants under 14 days, children from 2 months to 4 years, school children from 6 to 12 years, boys and girls from 13 to 19 years, adults from 22 to 39 years, a midde aged group from 42 to 60 years and persons from 62 to 90 years. The data for each patient are given and analyzed in terms of age and sex. In these groups the average red blood cell volume, anisocytosis and poikilocytosis ran parallel to the average diameter. In boys at puberty the average diameter was slightly larger than that of the erythrocytes of the girls. Cell thickness was slightly increased during the 6 to 12 year period. After puberty (most marked in the 20 to 40 year group) the red blood cell count and hemoglobin percentage were higher in men than in women, although in old age the difference was not considered significant mathematically. The red blood cell diameter was largest during the first two weeks of life, smallest during the period of 2 months to 4 years and in the adult range after puberty. The monograph is illustrated with twenty-one graphs and twenty-six tables, and an extensive bibliography is appended. It is an excellent reference work on normal blood.

Practical Methods in Biochemistry. By Frederick C. Koch, Frank P. Hixon Distinguished Service Professor of Biochemistry, University of Chicago, Chicago. Third edition. Cloth. Price, $2.25. Pp. 314, with 15 illustrations, Baltimore: William Wood & Company, 1941.

This edition of a laboratory manual for medical students carries forward the high ideals and scholarship of previous editions. New methods on uric, lactic and pyruvic acids are added. Extension to include qualitative and quantitative experiments on vitamins and hormones was considered but omitted because of the costly equipment necessary to insure results commensurate with the time and energy spent. This consideration of the student, in a field in which the author is a distinguished contributor, shows the soundness of his judgment and ideals: What cannot be done well, do not attempt. The author realizes that the student who brings much to a subject gets more out of it. He expects the user of the book to have sound fundamental training in chemistry, physics and biology. With this equipment this manual is well suited to guide him in biochemistry. The methods are given in clear and accurate terms. The illustrations of the more complicated apparatus are excellent and explanatory. The contents of the book are divided into three parts: (1) the chemistry of cell constituents, (2) the chemistry of the digestive tract and (3) blood and urine. The student who uses this manual as the instructions direct has every opportunity to become familiar with modern biochemistry. Those who wish a review in biochemical methods will find it a source of enlightenment.

Diseases of the Veins and Lymphatics of the Lower Extremity: A Manual of Veins and Lymphatics of the Lower Extremity for Students and Practitioners. By C. H. Verovitz, M.D., Demonstrator of Surgery, Western Reserve University School of Medicine, Cleveland. Cloth. Price, $6. Pp. 392, with illustrations. Boston: Christopher Publishing House, 1941.

This monograph contains much valuable material and many useful diagrams described by an author with obvious clinical experience and a keen power of observation. The poor organization of the subject matter, the loose grammar, the faulty spelling of names and the careless list of references, with titles and journals frequently misquoted, greatly detract from the value of the book. With careful editing and better organization, future editions might provide easier and more profitable reading.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SULFONAMIDE DRUGS IN SINUSITIS

***To the Editor:*—I read in The Journal that a 5 per cent solution of sodium sulfathiazole is useful in the treatment of sinus trouble. I read later that this solution is alkaline and irritating. May I ask whether sulfanilamide or azosulfamide is effective as a spray when used in the same way and, if so, in what per cent solution? Are solutions of these irritating? Also I should like to ask whether sulfanilamide or sulfathiazole powder would be effective if blown into the nose with a powder blower, and, if so, whether it would be irritant or contraindicated in any way?**

R. P. Little, M.D., New York.

ANSWER.—There is little evidence that a 1 per cent solution of sulfanilamide in physiologic solution of sodium chloride or that a 5 per cent solution of azosulfamide is of value as a spray or as an irrigating solution in the treatment of sinusitis. It is not likely that either solution would be irritating to the mucous membranes of the nose and throat. There are no reports concerning the introduction of sulfanilamide or sulfathiazole powder into the nose by means of a powder blower, although these drugs in a finely powdered form have been used as a medicinal snuff in attempts to eliminate hemolytic streptococci and staphylococci from the nasal passages. When these drugs have been used in this manner there have been mild degrees of irritation (such as slight itching and burning of the nasal mucous membranes and a watery discharge) noted. There are no extensive reports regarding the effectiveness of the powdered sulfanilamide or sulfathiazole in the control of sinus infections.

MANNITOL HEXANITRATE AS VASODILATOR

***To the Editor:*—It has recently come to my attention that mannitol hexanitrate is being advocated for use as a vasodilator in competition with erythrol tetranitrate, glyceryl trinitrate, sodium nitrite and even bismuth subnitrate. Where should one classify the usefulness of mannitol hexanitrate in comparison with other vasodilators and how does it compare with them in rapidity and duration of action?**

David Stein, M.D., Philadelphia.

ANSWER.—All the compounds listed in the question depend for their action on the liberation of the nitrite ion within the body. This action consists in a relaxation of smooth muscle tissue and is independent of innervation. Mannitol hexanitrate has never come into general use in the practice of medicine despite the fact that it has been known as a vasodilator for many years and has been recently revived. The reasons for this are that it is inferior to glyceryl trinitrate (nitroglycerin) and amyl nitrite for quick effect and to sodium nitrite for intermediate effect (relatively slow initial but more prolonged action) and apparently is little or no better and no less toxic than erythrol tetranitrate for an effect that lasts for hours. Goodman and Gilman (The Pharmacological Basis of Therapeutics, New York, Macmillan Company, 1941, p. 552) have published a table listing the characteristics of the vasodepressor response of hypertensive patients receiving full therapeutic doses of certain preparations which release the nitrite ion in the body. The substance of this table can be summarized as follows:

	Fall Begins, Minutes	Maximal Fall Reached, Minutes	Extent of Fall,* Mm. of Mercury	Time of Recovery, Minutes
Amyl nitrite	½-1	2-3	15-25	4-8
Glyceryl trinitrate	1-2	5-10	15-30	25-40
Sodium nitrite	5-20	25-40	25-40	60-150
Erythrityl tetranitrite	15-30	30-50	30-40	180-300
Mannitol hexanitrite	15-30	60-120	30-40	240-360

* Systolic blood pressure.

It is true, however, that mannitol hexanitrate has not, at least in recent years, had the clinical trial that the other nitrites have had. Further experience might or might not reveal a value not now known; disappointment in the clinical applicability of erythrol tetranitrate suggests, however, the probability of similar disappointment in the practical use of mannitol hexanitrate.

TREATMENT OF TRACHOMA

***To the Editor:*—Will you kindly send me information on the treatment of trachoma with sulfanilamide? What other treatment is indicated?**

Eleanor T. Calverley, M.D., Hartford, Conn.

ANSWER.—The treatment of trachoma with sulfanilamide and its congeners, originally described by Fred Loe of the Indian Medical Service, was said by Edward Jackson, the dean of American ophthalmologists, to be the greatest advance in the therapy of that disease in two thousand years. Interestingly enough, Loe's original technic of giving ½ grain (0.02 Gm.) of the drug by mouth per pound of body weight in twenty-four hours has never been improved on. Three courses of five to seven days each with an intervening rest period of three days suffice in nearly all cases. The blood level of sulfanilamide should be maintained during that time at between 3 and 4 mg., and naturally all precautions as to bodily health should be observed. No local treatment need accompany the internal use of the drug except a nonirritating cleansing solution to keep the conjunctival sac free from secretion.

Practically 75 to 90 per cent of cases of trachoma in stages 1 and 2 may be cured. Although there is an immediate relief of subjective symptoms, objective subconjunctival hyperplasias require from six weeks to six months to disappear and final judgment should not be passed until at least one year has elapsed. But of even greater importance than the cure is the fact proved by Thygeson that the disease cannot be transmitted after four days' use of sulfanilamide.

In stages 3 and 4 in which scar tissue contraction has occurred, brilliant results cannot be expected. Relief from secondary infection and relief from the pain of corneal trachoma are accomplished and the patient is made confortable. The disease is no longer susceptible of transmission, but the usual local measures are necessary because of the scarring.

IONTOPHORESIS FOR FUNGOUS INFECTION OF NAILS

***To the Editor:*—Hos copper iontophoresis ever been used in the treatment of fungous infections of the toenails? What were the results?**

M.D., London, Ky.

ANSWER.—Although Lowenfish treated 10 cases of dematophytosis by "cataphoresis" employing various fungicides, among which was copper, he concluded that the method was of "no value." Subsequent investigations by Haggard, Strauss and Greenberg and by Hoechstetter indicate that copper iontophoresis is valuable in treatment for fungous infections of the hands and feet.

Haggard and his associates found that 26 of 37 patients obtained "clinical cure"; and Hoechstetter, using the same method, reported that 16 of 18 cases of fungous infection of the feet were "clinically healed" following copper iontophoresis.

Gunderson reported that he employed iontophoresis only if other methods failed and said that his experience suggested that there were no contraindications to the use of copper iontophoresis. Gunderson recommended copper iontophoresis as the treatment of choice in stubborn cases and used it in preference to roentgen therapy. However, he resorted to the use of iontophoresis only if other methods failed.

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Haggard, H. W.; Strauss, M. J., and Greenberg, L. A.: Fungous Infections of the Hands and Feet Treated by Iontophoresis of Copper (Preliminary Report), THE JOURNAL, April 1, 1939, p. 1229.

Hoechstetter, S. S.: Fungous Infection of the Feet Treated by Copper Iontophoresis, *Mil. Surgeon* **87:** 50 (July) 1940.

Gunderson, G. O.: Iontophoresis, *Indust. Med.* **9:** 405 (Aug.) 1940.

USE OF BLOOD FOR PREGNANCY TEST

***To the Editor:*—Would you tell me what are the comparative merits of using blood instead of urine for the Friedman test for pregnancy? I have in mind the Hofmann modification of the Friedman test, in which from 10 to 13 cc. of blood serum which has been extracted with ether is injected intravenously in the test rabbit, and autopsy performed in twenty-four to thirty-six hours. Reference to this test may be found in the *Journal of Laboratory and Clinical Medicine* 22: 508 (Feb.) 1937**

T. T. Rackliffe, M.D., Los Angeles.

ANSWER.—The test referred to is a recognized procedure which gives excellent results. The advantages over the Friedman test are those of speed and availability of a sufficient amount of hormone in the blood at any time of day. With the serum recovered from about 12 cc. of blood, a result can be read macroscopically in twenty-four hours. The blood may be drawn at any time of the day without respect to meals or other factors, while in the urine test a morning specimen after restricting fluid intake for twelve hours is most satisfactory.

The only objection to the use of serum is that there is a greater chance of obtaining a toxicity from this material. Because of this there may be a higher rate of mortality among the test animals, probably as a result of protein shock from the serum used. The washing of the serum with ether is a step in the reduction of test animal mortality, as the ether acts to detoxify the serum.

Details of the technical procedure involved may be found in Clinical Laboratory Methods and Diagnosis by R. B. H. Gradwohl, published by the C. V. Mosby Company.

SYPHILOPHOBIA OR SYPHILIS WITH NEGATIVE SEROLOGIC REACTIONS

To the Editor:—Please inform me whether any cases of syphilis in which the serologic reaction is persistently negative are known and how they may be explained. I have a syphilophobe under treatment whom I am trying to convince that he is free of the disease but who persists in believing that his is a rare case because the reaction of the blood serum is consistently negative, a condition which I had to admit is theoretically possible although I have never seen it. To the best of my knowledge a consistently negative Wassermann, Kahn or Kolmer reaction, or preferably a combination of these, is, in the absence of clinical symptoms of syphilis, positive proof of the absence of syphilitic infection.

R. W. Mueller, M.D., Los Angeles.

ANSWER.—Yes, it is possible for a person with syphilis to have a persistently negative serologic reaction. So-called burnt out tabes is a good example of this. Unfortunately, there is not enough information on this patient to assist much in formulating an answer. Did the patient ever have syphilis? That is the first thing to decide. If the patient has had a consistently negative Wassermann, Kahn or Kolmer test, or a combination of these, with an absence of clinical symptoms of syphilis, then there seems to be no reason why he should be treated.

On the other hand, if the patient has had syphilis, then he must have had sufficient continuous therapy, with alternating courses of an arsenical and of a bismuth compound for a year to eighteen months; his blood serologic reactions must have been negative for at least a year; lumbar puncture must give negative results, and the examination of the cardiovascular system must show no evidence of syphilitic involvement in order to warrant the stopping of therapy.

Unfortunately, the physician does encounter patients with syphilophobia who will take treatment just as long as they can get the physician to give it to them. Such patients are really a problem for the psychiatrist.

PROGNOSIS IN PAROXYSMAL TACHYCARDIA AND QUINIDINE

To the Editor:—1. A man of 22 has had attacks of paroxysmal auricular tachycardia since the age of 12, now occurring about once a week. These attacks he controls by holding his breath and bending over. Physical examination is essentially negative except for his excessive height, 6 feet 4 inches (193 cm.), and low weight, 145 pounds (66 Kg.). There is no past history suggestive of any etiologic factors for heart disease on physical examination or from his system review. Would you please tell me if I am correct in giving him a good prognosis?

M.D., Massachusetts.

2. A woman of 29, otherwise in good health, has had disturbing attacks of paroxysmal auricular tachycardia, confirmed by electrocardiogram, for about four years. At first these were as frequent as ten or fifteen a day, but she has responded well to quinidine, 20 grains (1.3 Gm.) daily. She has two bad wisdom teeth, which may have a bearing on the condition. She has asked me whether she will ever recover completely from the attacks, and I have been unable to find any answer to her question. When this arrhythmia is present without other illnesses (that is, in healthy young adults), what is the likelihood of spontaneous cessation of attacks, and does medication such as quinidine (which controls this patient's attacks) have any permanent effect in stopping the attacks?

E. C. Heyde, M.D., Wooster, Ohio.

ANSWER.—1. From the facts given it would appear that a good prognosis is entirely warranted. There is a fair likelihood that the number and severity of the patient's attacks will decrease as the years pass, but even if this does not occur they will probably not prove incapacitating.

2. A fairly large number of young patients with paroxysmal tachycardia who are otherwise healthy recover spontaneously. Reliable figures are not available, in part because many such patients probably fail to come under the care of physicians. There is no evidence that quinidine has any permanent effect in stopping the attacks. In some patients so treated the attacks do not recur after cessation of therapy, but as indicated the tendency frequently stops spontaneously and the efficacy of the quinidine cannot be proved. In this connection, because quinidine acts by virtue of being a protoplasmic poison, it would seem wise to stop it at intervals in the hope that spontaneous recovery may have occurred. This is especially true if as much as 1.3 Gm. of quinidine a day is necessary to control the attacks.

KNOCK KNEES IN YOUNG CHILD

To the Editor:—Can you please give me information on the treatment of knock knees in a child of three years and eight months? The condition is of rachitic origin. The child has been receiving 10 drops of percomorph liver oil twice daily since July, 1939. At times he urinates too frequently; should the dose be decreased? His height is 41¼ inches and his weight is 48 pounds. Is it possible that the deformity will decrease as the leg lengthens?

M.D., Canada.

ANSWER.—If the knock knee is not produced by some generalized disturbance such as rickets or osteodystrophy the treatment would depend to some extent on the severity of the deformity. If the deformity is mild a slight change in the weight-bearing thrust obtained by applying Thomas heels wedged 3/16 inch (0.48 cm.) on the inner side of the shoes will frequently bring about gradual correction. If there is evidence that the percomorph liver oil is causing some renal irritation, it would be well to change to some other form of vitamin D. Massive doses are not indicated unless there is evidence of a real rachitic change in the bone. If the deformity is severe, osteotomy of the lower end of the femur or the upper end of the tibia, depending on where the malalinement is most evident, would be justifiable. It is impossible to state whether the knock knee tendency will improve or increase as the thigh lengthens without knowing more about what has caused it. In the average patient mild knock knee can be corrected, however, with the simple shoe correction in addition to a maintenance dose of vitamin D.

REHABILITATION OF THE DEAF

To the Editor:—I note in the St. Louis press the recent death of Dr. M. A. Goldstein. Dr. Goldstein established the Central Institute for the Deaf, in embryo, about twenty-five years ago. It has grown to be a successful school. I have been out of the practice of medicine for at least ten years and have not kept pace with the latest advances in restoring the hearing in those congenitally deaf or the victims of such resistant and intractable afflictions as otosclerosis or traumatic deafness. Will you please tell me just what supposed permanent advancement in otologic science Dr. Goldstein is credited with—whether physiologic, electric or mechanical? The St. Louis press leaves one to understand that originality and creativeness are involved in the methods in use in the institute.

M.D., Louisiana.

ANSWER.—Dr. Goldstein's interest and activities were directed chiefly toward the teaching and rehabilitation of the deaf person rather than to the treatment of deafness. He originated no methods of "restoring hearing in the congenitally deaf or in those afflicted with otosclerosis or traumatic deafness." His views on the management of the deaf child are expounded in Goldstein, Max Aaron: The Acoustic Method for the Training of the Deaf and Hard of Hearing Child, St. Louis, Laryngoscope Press, 1939.

CONTROL OF HEMORRHAGE AFTER TONSILLECTOMY

To the Editor:—I have heard that equal parts of gallic acid and tannic acid are good to control hemorrhage with after tonsillectomies. Is this true, and, if so, what strength of the two acids is used?

Joseph P. Sparks, M.D., Manito, Ill.

ANSWER.—It is true that gallic and tannic acids are useful in the control of hemorrhage after tonsillectomy. They should be used, however, only for the control of minor hemorrhage. Severe bleeding from large vessels should be handled as it is in other branches of surgery, namely by means of pressure, clamping and the ligature.

A 1 ounce medicine glass is filled with gallic acid or tannic acid crystals, separately or in equal amounts, and enough epinephrine hydrochloride 1:1,000 in physiologic solution of sodium chloride should be added, drop by drop, until a paste of the consistency of mustard is obtained. The whole should be stirred as it is prepared. Tannic and gallic acids are easily soluble in this solution and too much should not be used, as the mixture then becomes too thin for efficient action.

PREGNANCY AND MÉNIÈRE'S DISEASE

To the Editor:—A woman aged 29 has been under my care for Ménière's disease for the past one and one-half years. Treatment with a low sodium Fürstenberg regimen, ammonium chloride and the use of histamine acid phosphate intravenously, as used at the Mayo Clinic, have been successfully employed. The patient has a child 5 years of age, having had a pregnancy five years ago that terminated normally and spontaneously. She is desirous of having another baby. Will this have a detrimental effect on the Ménière's disease?

M.D., New York.

ANSWER.—While any metabolic disturbance may cause an exacerbation of Ménière's disease, if the patient has been free from symptoms for some time there is not a great likelihood of trouble from pregnancy. Ménière's disease tends to run a self-limited course, and the patient may now be past the stage of severe attacks of vertigo.